10/750,743

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS	4	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	5	SEP 01	New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS	6	SEP 27	STANDARDS will no longer be available on STN
NEWS	7	SEP 27	SWETSCAN will no longer be available on STN
NEWS	8	OCT 28	KOREAPAT now available on STN
NEWS	9	NOV 18	Current-awareness alerts, saved answer sets, and current search transcripts to be affected by CERAB, COMPUAB, ELCOM, and SOLIDSTATE reloads
NEWS	10	NOV 30	PHAR reloaded with additional data
NEWS	11	DEC 01	LISA now available on STN

NEWS EXPRESS	OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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FILE 'HOME' ENTERED AT 17:50:50 ON 06 DEC 2004

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 17:50:54 ON 06 DEC 2004
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Property values tagged with IC are from the ZIC/VINITI data file
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STRUCTURE FILE UPDATES: 5 DEC 2004 HIGHEST RN 792236-36-3
DICTIONARY FILE UPDATES: 5 DEC 2004 HIGHEST RN 792236-36-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

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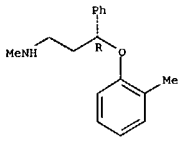
Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> s atomoxetine/cn
L1   1 ATOMOXETINE/CN

=> d l1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 83015-26-3 REGISTRY
CN Benzenepropanamine, N-methyl-γ-(2-methylphenoxy)-, (γR)- (9CI)
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Benzenepropanamine, N-methyl-γ-(2-methylphenoxy)-, (R)-
OTHER NAMES:
CN (-)-Tomoxetine
CN **Atomoxetine**
CN Tomoxetine
FS STEREOSEARCH
MF C17 H21 N O
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study)

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

109 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
109 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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=> fil caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         7.46       7.67

FILE 'CAPLUS' ENTERED AT 17:52:29 ON 06 DEC 2004
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FILE COVERS 1907 - 6 Dec 2004  VOL 141 ISS 24
FILE LAST UPDATED: 5 Dec 2004  (20041205/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


=> s atomox?
L2          50 ATOMOX?

=> s atomoxetine
L3          50 ATOMOXETINE

=> s 83015-26-3/rn
           109 83015-26-3
             3 83015-26-3D
L4         107 83015-26-3/RN
                 (83015-26-3 (NOTL) 83015-26-3D )

=> s 83015-26-3D/rn
L5           3 83015-26-3D/RN
                 (83015-26-3D)

=> s l4 or l5
L6         109 L4 OR L5

=> s sex?
L7      143300 SEX?

=> s l6 and l7
L8           3 L6 AND L7

=> d l8 1-3 abs ibib hitstr
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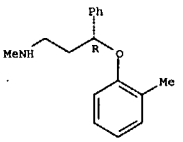
L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AB A review. Atomoxetine is the first nonstimulant drug approved by the United States Food and Drug Administration (FDA) for the treatment of attention-deficit-hyperactivity disorder (ADHD), and the only agent approved by the FDA for the treatment of ADHD in adults. Atomoxetine is a norepinephrine transport inhibitor that acts almost exclusively on the noradrenergic pathway. Its mechanism of action in the control and maintenance of ADHD symptoms is thought to be through the highly specific presynaptic inhibition of norepinephrine. Clin. trials to evaluate the short-term effects of atomoxetine in children and adults have shown that atomoxetine is effective in maintaining control of ADHD. Likewise, long-term trials have determined that atomoxetine is effective in preventing relapse of ADHD symptoms without an increase in adverse effects. A comparative trial of atomoxetine with methylphenidate in school-aged children indicated similar safety and efficacy without the abuse liability associated with some psychostimulants. The most commonly reported adverse effects in children and adolescents are dyspepsia, nausea, vomiting, decreased appetite, and weight loss. The rates of adverse events in the trials were similar for both the once- and twice-daily dosing regimens. The discontinuation rate was 3.5% in patients treated with atomoxetine vs. 1.4% for placebo and appeared to be dose dependent, with a higher percentage of discontinuation at dosages greater than 1.5 mg/kg/day. In clin. trials involving adults, the emergence of clin. significant or intolerable adverse events was low. The most common adverse events in adults were dry mouth, insomnia, nausea, decreased appetite, constipation, urinary retention or difficulties with micturition, erectile disturbance, dysmenorrhea, dizziness, and decreased libido. **Sexual** dysfunction occurred in approx. 2% of patients treated with atomoxetine. Atomoxetine should be used with caution in patients who have hypertension or any significant cardiovascular disorder. Overall, atomoxetine therapy in patients with ADHD appears to be effective in controlling symptoms and maintaining remission, with the advantages being comparable efficacy with that of methylphenidate, a favorable safety profile, and non-controlled substance status. Addnl. long-term studies are needed to determine its continued efficacy for those who require lifelong treatment, and comparative trials against other stimulant and nonstimulant agents.

ACCESSION NUMBER: 2004:719696 CAPLUS
DOCUMENT NUMBER: 141:306872
TITLE: Atomoxetine, a novel treatment for attention-deficit-hyperactivity disorder
AUTHOR(S): Christman, Alisa K.; Fermo, Joli D.; Markowitz, John S.
CORPORATE SOURCE: Departments of Pharmacy Practice, Medical University of South Carolina, Charleston, USA
SOURCE: Pharmacotherapy (2004), 24(8), 1020-1036
CODEN: PHPYDQ; ISSN: 0277-0008
PUBLISHER: Pharmacotherapy Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

IT **83015-26-3**, Atomoxetine
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(atomoxetine for attention-deficit-hyperactivity disorder)

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 83015-26-3 CAPLUS
CN Benzenepropanamine, N-methyl-γ-(2-methylphenoxy)-, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

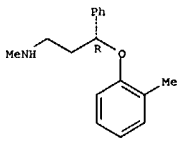
L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
AB Background and Objectives: Atomoxetine is a treatment for attention-deficit/hyperactivity disorder and is primarily eliminated via cytochrome P 4502D6 (CYP2D6). The pharmacokinetics of atomoxetine and its primary metabolites were investigated in 10 adults with hepatic impairment (6 moderate, 4 severe) and 10 age- and **sex**-matched control subjects, all being genotyped as CYP2D6 extensive metabolizers. Methods: A single oral 20-mg dose of atomoxetine was given. Multiple blood samples were collected for 48 h in healthy subjects and for 120 h in patients. Urine was collected up to 24 h. Before atomoxetine administration (10-20 days), sorbitol clearance and debrisoquin (INN, debrisoquine) metabolic ratio were determined as markers of hepatic blood flow and CYP2D6 activity, resp. Results: The systemic clearance of atomoxetine was significantly reduced in those with hepatic impairment compared with controls, thereby resulting in increased exposure (area under the concentration-time curve from time 0 to infinity, 1.58 vs. 0.85 μg · h-1 · mL-1; P =.035) but no change in maximum concentration Mean 4-hydroxyatomoxetine area under the concentration-time curve from time 0 to time t and maximum concentration were increased approx. 7-fold and 2-fold, resp. (P =.0001 and P =.0056, resp.). For the glucuronide conjugate of 4-hydroxyatomoxetine, the mean half-life was longer and the mean area under the concentration-time curve from time 0 to infinity and the maximum concentration were lower (P =.0028, P =.003, and P =.0001, resp.). The sorbitol clearance was lower and the debrisoquin metabolic ratio was higher, reflecting reduced hepatic blood flow and decreased CYP2D6 activity, resp. Decreased atomoxetine clearance in patients with hepatic impairment was clearly correlated with decreased CYP2D6 activity and decreased hepatic blood flow. Mean atomoxetine plasma protein binding was lower in patients with hepatic impairment compared with controls (96.5% vs. 98.7%, P =.0008). Atomoxetine was well tolerated in the 2 populations. Conclusion: For patients with attention-deficit/hyperactivity disorder who have hepatic impairment, dosage adjustment is recommended. Initial target doses should be reduced to 25% and 50% of the normal dose for patients with severe and moderate hepatic impairment, resp.

ACCESSION NUMBER: 2003:212349 CAPLUS
DOCUMENT NUMBER: 139:316551
TITLE: Effect of hepatic impairment on the pharmacokinetics of atomoxetine and its metabolites
AUTHOR(S): Chalon, Stephan A.; Desager, Jean-Pierre; DeSante, Karl A.; Frye, Reginald F.; Witcher, Jennifer; Long, Amanda J.; Sauer, John-Michael; Golnez, Jean-Luc; Smith, Brian P.; Thomasson, Holly R.; Horsmans, Yves
CORPORATE SOURCE: Lilly Res. Lab., Indianapolis, IN, USA
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (2003), 73(3), 178-191
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **83015-26-3**, Atomoxetine

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(effect of hepatic impairment on pharmacokinetics of atomoxetine and its metabolites in relation to CYP2D6 genotype)
RN 83015-26-3 CAPLUS
CN Benzenepropanamine, N-methyl-γ-(2-methylphenoxy)-, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

AB A composition comprising: (a) a pharmaceutically effective amount of one or more norepinephrine reuptake inhibitors or a salt; and (b) 1 or more neuroleptics is provided. The composition is useful in treating disorders or diseases of the central nervous system, and particularly useful in treating schizophrenia. A pharmaceutical composition was prepared by combining reboxetine with a neuroleptic in an acceptable carrier. The composition contains 0.01-10 mg rebexetine and 25-300 mg clozapine.

ACCESSION NUMBER: 2002:521465 CAPLUS
DOCUMENT NUMBER: 137:98994
TITLE: Pharmaceuticals containing a combination of norepinephrine reuptake inhibitors and neuroleptics
INVENTOR(S): Wong, Erik Ho Fong; Gallen, Christopher C.; Svensson, Torgny
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA; Pharmacia AB
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

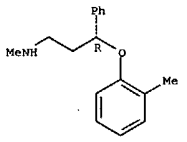
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053140	A2	20020711	WO 2001-US45871	20011227
WO 2002053140	A3	20021024		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2431041	AA	20020711	CA 2001-2431041	20011227
EP 1353675	A2	20031022	EP 2001-991997	20011227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004517112	T2	20040610	JP 2002-554091	20011227
US 2002156067	A1	20021024	US 2001-35100	20011228
PRIORITY APPLN. INFO.:			US 2001-259286P	P 20010102
			WO 2001-US45871	W 20011227

IT **83015-26-3**, Tomoxetine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals containing combination of norepinephrine reuptake inhibitors and neuroleptics)

RN 83015-26-3 CAPLUS
CN Benzenepropanamine, N-methyl-γ-(2-methylphenoxy)-, (γR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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     (FILE 'HOME' ENTERED AT 17:50:50 ON 06 DEC 2004)

     FILE 'REGISTRY' ENTERED AT 17:50:54 ON 06 DEC 2004
L1             1 S ATOMOXETINE/CN

     FILE 'CAPLUS' ENTERED AT 17:52:29 ON 06 DEC 2004
L2            50 S ATOMOX?
L3            50 S ATOMOXETINE
L4           107 S 83015-26-3/RN
L5             3 S 83015-26-3D/RN
L6           109 S L4 OR L5
L7        143300 S SEX?
L8             3 S L6 AND L7

=> s l6 not l8
L9           106 L6 NOT L8

=> d l9 1-106 abs ibib
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L9 ANSWER 1 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The invention relates to a method of treating at least one symptom of a lower urinary tract disorder in a subject in need of treatment wherein the symptom is selected from the group consisting of urinary frequency, urinary urgency, urinary urge incontinence, nocturia and enuresis. The method comprises administering to a subject in need of treatment a therapeutically effective amount of a compound that has 5-HT3 receptor antagonist activity and NorAdrenaline Reuptake Inhibitor (NARI) activity. The invention further relates to a method of treating at least one symptom of a lower urinary tract disorder in a subject in need of treatment wherein the symptom is selected from the group consisting of urinary frequency, urinary urgency, urinary urge incontinence, nocturia and enuresis, comprising coadministering to said subject a first amount of a 5HT3 antagonist and a second amount of a NARI, wherein the first and second amts. together comprise a therapeutically effective amount or are each present in a therapeutically effective amount Administration of MCI-225 to rat or cat models of overactive bladder caused a significant dose-dependent increase in bladder capacity.

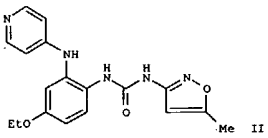
ACCESSION NUMBER: 2004:878266 CAPLUS
DOCUMENT NUMBER: 141:343543
TITLE: Method of treating lower urinary tract disorders with 5-HT3 receptor antagonist and noradrenaline reuptake inhibitor combination
INVENTOR(S): Landau, Steven B.; Miller, Cheryl L.; Fraser, Matthew O.
PATENT ASSIGNEE(S): Dynogen Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089288	A2	20041021	WO 2004-US10088	20040402
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004209869	A1	20041021	US 2004-817332	20040402

PRIORITY APPLN. INFO.: US 2003-461022P P 20030404
US 2003-496502P P 20030820
US 2004-536341P P 20040113

L9 ANSWER 2 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

GI



II

AB The invention provides di(hetero)arylureas A-NH-C(:X)-NH-B [I; X = O or S; A = certain (un)substituted 6-membered (hetero)aryl rings containing 0-4 N atoms, e.g., Ph, pyridinyl; B = certain (un)substituted 5- or 6-membered (hetero)aromatic rings containing O, NH or derivs., N, or S, particularly 6-membered rings with 0-4 N as cited of A, or 5-membered azole-type heterocycles bound at C or N]. These compds. may be in the form of pharmaceutical salts or compns., or may be in pure enantiomeric form or racemic mixts. I are useful in pharmaceuticals used to treat a wide variety of diseases or conditions in which the α7 subunit of the nicotinic acetylcholine receptor (α7nAChR) is known to be involved. I may be used in combination with a variety of other agents, including antipsychotics, agents which increase brain acetylcholine levels, or which inhibit acetylcholinesterase, or which activate production of acetylcholine, or monoamine reuptake inhibitors, psychostimulants, or α7nAChR agonists. A total of 25 compds. are described, 23 with preparatory details. Using a FLIPR, cell-based, Ca flux assay with mutated α7nAChR expressed in SHEP-1 cells, the example compds. had activity between 10 nM and 10 μM. For instance, invention compound II was prepared in 4 steps. Thus, ethanolysis of 2-bromo-4-fluoro-1-nitrobenzene with NaOEt in EtOH (68%), and Pd complex-catalyzed coupling of the resultant 2-bromo-4-ethoxy-1-nitrobenzene with 4-aminopyridine (84%) gave N-(5-ethoxy-2-nitrophenyl)pyridin-4-amine. Hydrogenation of the nitro group to amino (89%) and carbamoylation by Ph (5-methylisoxazol-3-yl)carbamate (81%) gave II.

ACCESSION NUMBER: 2004:817889 CAPLUS
DOCUMENT NUMBER: 141:332200
TITLE: N,N'-Di(hetero)aryl(thio)ureas useful as positive allosteric modulators of the α7 subunit of the nicotinic acetylcholine receptor, and their pharmaceutical compositions, uses, and preparation
INVENTOR(S): Rogers, Bruce Nelsen; Piotrowski, David Walter; Margolis, Brandon Jerome; Myers, Jason Kenneth; Groppi, Vincent Edward, Jr.; Rudmann, Daniel Gregory
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

L9 ANSWER 2 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004085433	A2	20041007	WO 2004-IB838	20040315
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2003-458766P P 20030328

L9 ANSWER 3 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The present invention relates to compositions and methods to treat diseases or conditions with alpha-7 nicotinic acetylcholine receptor (AChR) full agonists by decreasing levels of tumor necrosis factor-alpha and/or by stimulating vascular angiogenesis.

ACCESSION NUMBER: 2004:633526 CAPLUS
DOCUMENT NUMBER: 141:167817
TITLE: Treatment of diseases with alpha-7 NACh receptor full agonists
INVENTOR(S): Groppi, Vincent Edward, Jr.; Rogers, Bruce Nelsen; Rudmann, Daniel Gregory
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004064836	A2	20040805	WO 2004-IB115	20040112
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ				

PRIORITY APPLN. INFO.: US 2003-441801P P 20030122

OTHER SOURCE(S): MARPAT 141:167817

L9 ANSWER 4 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review. Atomoxetine (Strattera, Eli Lilly & Co.) is a highly selective noradrenaline reuptake inhibitor and the first nonstimulant medication to be approved for the treatment of attention deficit hyperactivity disorder.
Currently, nine published clin. trials have documented the safety and efficacy of atomoxetine in the treatment of children, adolescents and adults with attention deficit hyperactivity disorder and data presented throughout the past year of national scientific meetings has further addressed its utility. This article reviews the available information on atomoxetine, accompanied by a discussion of its clin. use.

ACCESSION NUMBER: 2004:630521 CAPLUS
DOCUMENT NUMBER: 141:235427
TITLE: Atomoxetine in the treatment of attention deficit hyperactivity disorder
AUTHOR(S): Kratochvil, Christopher J.; Vaughan, Brigette S.; Daughton, Joan M.; Mayfield-Jorgensen, Michelle L.; Burke, William J.
CORPORATE SOURCE: 985581 Nebraska Medical Center, University of Nebraska
Medical Center, Omaha, NE, 68198 5581, USA
SOURCE: Expert Review of Neurotherapeutics (2004), 4(4), 601-611
CODEN: ERNXAR; ISSN: 1473-7175
PUBLISHER: Future Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The invention relates to a method of treating nausea, vomiting, retching or any combination thereof in a subject in need of treatment. The method comprises administering to a subject in need of treatment a therapeutically effective amount of a compound that has 5-HT3 receptor antagonist activity and NorAdrenaline Reuptake Inhibitor (NARI) activity. The invention further relates to a method of treating nausea, vomiting, retching or any combination thereof in a subject in need thereof, comprising coadministering to said subject a first amount of a 5-HT3 antagonist and a second amount of a NARI, wherein the first and second amts. together comprise a therapeutically effective amount or are each present in a therapeutically effective amount In addition, the method of the invention comprises administering a NARI alone. A pharmaceutical composition comprising: (a) a first amount of a 5-HT3 receptor antagonist; and (b) a second amount of a noradrenaline reuptake inhibitor is also claimed.

ACCESSION NUMBER: 2004:610068 CAPLUS
DOCUMENT NUMBER: 141:134099
TITLE: Method of treating nausea, vomiting, or retching by administering a 5-HT3 receptor antagonist and noradrenaline reuptake inhibitor
INVENTOR(S): Landau, Steven B.; Miller, Cheryl L.; Thor, Karl Bruce
PATENT ASSIGNEE(S): Dynogen Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004062624	A2	20040729	WO 2004-US809	20040113
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ				
US 2004147510	A1	20040729	US 2004-757981	20040113
PRIORITY APPLN. INFO.:			US 2003-440076P	P 20030113
			US 2003-492478P	P 20030804

OTHER SOURCE(S): MARPAT 141:134099

L9 ANSWER 6 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The invention relates to a method of treating functional bowel disorders in a subject in need of treatment. The method comprises administering to a subject in need of treatment a therapeutically effective amount of a compound that has 5-HT3 receptor antagonist activity and NorAdrenaline Reuptake Inhibitor (NARI) activity. The invention further relates to a method of treating a functional bowel disorder in a subject in need thereof, comprising coadministering to said subject a first amount of a 5-HT3 antagonist and a second amount of a NARI, wherein the first and second amts. together comprise a therapeutically effective amount or are each present in a therapeutically effective amount In addition, the method of the invention comprises administering a NARI alone. The functional bowel disorders which can be treated according to the method of the invention include IBS, functional abdominal bloating, functional constipation and functional diarrhea. A pharmaceutical composition comprising: (a) a first amount of a 5-HT3 receptor antagonist; and (b) a second amount of a noradrenaline reuptake inhibitor is also claimed.

ACCESSION NUMBER: 2004:610067 CAPLUS
DOCUMENT NUMBER: 141:134098
TITLE: Method of treating functional bowel disorders by administering a 5-HT3 receptor antagonist and noradrenaline reuptake inhibitor
INVENTOR(S): Landau, Steven B.
PATENT ASSIGNEE(S): Dynogen Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004062623	A2	20040729	WO 2004-US807	20040113
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ				
US 2004147509	A1	20040729	US 2004-757364	20040113
PRIORITY APPLN. INFO.:			US 2003-440077P	P 20030113
			US 2003-492480P	P 20030804

OTHER SOURCE(S): MARPAT 141:134098

L9 ANSWER 7 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A method of treating, preventing, or inhibiting a CNS disorder and/or pain and inflammation or an inflammation-associated disorder in a subject in need of such treatment or prevention provides for treating the subject with duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor or prodrug thereof, wherein the amount of duloxetine, venlafaxine or atomoxetine and the amount of a cyclooxygenase-2 selective inhibitor or prodrug thereof together constitute a CNS disorder, pain and inflammation, or inflammation-associated disorder suppressing treatment, prevention, or inhibition effective amount of the composition Compns. and pharmaceutical compns. that contain duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor are also disclosed.

ACCESSION NUMBER: 2004:589414 CAPLUS
DOCUMENT NUMBER: 141:134107
TITLE: A method for the treatment, prevention, or inhibition of a CNS disorder and/or pain and inflammation using a combination of duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor and compositions thereof
INVENTOR(S): Arneric, Stephen P.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060366	A1	20040722	WO 2003-US38751	20031206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004235925	A1	20041125	US 2003-727717	20031204
PRIORITY APPLN. INFO.:			US 2002-433790P	P 20021217

OTHER SOURCE(S): MARPAT 141:134107

L9 ANSWER 8 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The major human metabolite of atomoxetine (4-hydroxyatomoxetine) was tested against a panel of receptors and enzymes, and was found to interact with the μ, δ, and κ-opioid receptors based upon studies involving both binding and functional assays. 4-Hydroxyatomoxetine was determined to be a partial agonist of the κ-opioid receptor.

ACCESSION NUMBER: 2004:523316 CAPLUS
DOCUMENT NUMBER: 141:133514
TITLE: Synthesis and biological evaluation of the major metabolite of atomoxetine: elucidation of a partial κ-opioid agonist effect
AUTHOR(S): Creighton, Christopher J.; Ramabadran, Kris; Ciccone, Patrick E.; Liu, Jingchun; Orsini, Michael J.; Reitz, Allen B.
CORPORATE SOURCE: Drug Discovery, Research and Development, Johnson and Johnson Pharmaceutical, Spring House, PA, 19477-0776, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(15), 4083-4085
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 9 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

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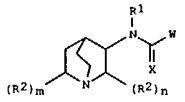

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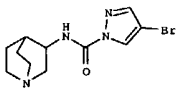

II

AB Title N-(1-azabicyclo[2.2.2]octyl)heteroarylamides I and analogs [wherein X = o, S; R1 = H, (halo)alkyl, cycloalkyl, substituted Ph, naphthyl; R2 = independently halo, cycloalkyl, aryl, (un)substituted alkyl; m = 0-1; n = 0-1; with the proviso that m + n = 1; W = (un)substituted Ph, heterocyclyl, heteroaryl; or pharmaceutically acceptable salts, racemic mixts., or pure enantiomers thereof] were prepared as α7 nicotinic acetylcholine receptor (nAChR) full agonists (no data). For example, reaction of phosgene with 4-bromopyrazole in EtOAc, followed by coupling with (+)-3-aminoquinuclidine•2HCl provided II•HCl (25%). The invention provides for compns. of I with psychostimulants and/or monoamine reuptake inhibitors for the treatment of attention deficit hyperactivity disorder (ADHD).

ACCESSION NUMBER: 2004:513575 CAPLUS
DOCUMENT NUMBER: 141:71755
TITLE: Preparation of N-(quinuclidinyl)heteroarylamides as nicotinic acetylcholine receptor agonists for use in combination therapy for the treatment of ADHD
INVENTOR(S): Groppi, Vincent Edward, Jr.; Jacobsen, Eric Jon; Myers, Jason Kenneth; Piotrowski, David Walter; Rogers, Bruce Nelsen; Walker, Daniel Patrick; Wishka, Donn Gregory
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004052461	A1	20040624	WO 2003-IB5542	20031128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

L9 ANSWER 9 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PRIORITY APPLN. INFO.: US 2002-432586P P 20021211

OTHER SOURCE(S): MARPAT 141:71755

L9 ANSWER 10 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB This invention describes a new combination for the treatment of urinary incontinence and urge urinary incontinence comprising a dual reuptake inhibitor of serotonin and/or - preferably and - norpinephrine and a beta-3-receptor agonist for the treatment of urinary incontinence.

ACCESSION NUMBER: 2004:446890 CAPLUS
DOCUMENT NUMBER: 141:12284
TITLE: Combination of a β3-receptor agonist and of a reuptake inhibitor of serotonin and/or norepinephrine for treatment of urinary incontinence
INVENTOR(S): Ebinger, Ursula; Mehlburger, Ludwig; Michel, Martin C.; Wienrich, Marion
PATENT ASSIGNEE(S): Boehringer Ingelheim International GmbH, Germany
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1424079	A1	20040602	EP 2002-26546	20021127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
WO 2004047830	A2	20040610	WO 2003-EP12225	20031103
WO 2004047830	A3	20040819		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004047838	A2	20040610	WO 2003-EP12331	20031105
WO 2004047838	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2002-26546 A 20021127

L9 ANSWER 11 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review. Special considerations arise in treating children and adolescents with antidepressants. Empirical data on antidepressants (and other pharmacol. agents) in young patients are quite limited. Psychiatrists, faced with depriving children of potentially effective medication or prescribing medications "off label," need information on which to base treatment decisions, and efforts are underway (e.g., by the National Institutes of Health, the American Academy of Pediatrics, and the Food and Drug Administration) to promote research in this area. Clin. significant differences in pharmacokinetics and possibly pharmacodynamics between adults and younger patients can also complicate treatment (e.g., younger patients may need higher doses on a milligram-per-kilogram basis to achieve the same drug concentration as an adult on a usually effective adult dose). Younger patients may also be more sensitive to adverse effects of medications. The selective serotonin reuptake inhibitors (SSRIs) have superceded tricyclic antidepressants (TCAs) as first-choice pharmacotherapy based on studies demonstrating their superior safety and efficacy in children with major depressive disorder (MDD). TCAs are now usually reserved for children or adolescents with at least moderate depression who have not responded to at least one newer antidepressant; it is recommended that therapeutic drug monitoring (TDM) of the TCA be done at least once to ensure that the patient does not develop toxic plasma levels. The safety, pharmacokinetics, and tolerability of venlafaxine and nefazodone have been tested in children, but data on efficacy are not yet available. The adverse effect profiles of the SSRIs, the TCAs, venlafaxine, and nefazodone are similar to those in adults. The TCA clomipramine and the SSRIs fluvoxamine and sertraline have indications for obsessive-compulsive disorder in pediatric patients. A number of TCAs and SSRIs have been studied in the treatment of other anxiety disorders (e.g., separation anxiety disorder, school phobia, elective mutism, generalized anxiety disorder) but none has received labeling for those indications. Antidepressants have been studied in the treatment of attention-deficit/hyperactivity disorder (ADHD). The TCA desipramine and bupropion have been found efficacious in ADHD, although desipramine causes higher rates of adverse effects than stimulant medications. Current treatment algorithms generally recommend trying an antidepressant after failed trials of several different stimulant medications. Atomoxetine, a nonstimulant medication, was recently approved for the treatment of ADHD in children, adolescents, and adults. Although behavioral management is preferred for treatment of enuresis, the TCA imipramine has also been found effective, although the relapse rate is as high as 50% upon discontinuation. Given the paucity of data on antidepressants in pediatric patients and the clin. significant pharmacokinetic differences between younger patients and adults, clinicians should carefully consider and cautiously monitor any treatment plan involving antidepressant medications in order to maintain the risk to benefit ratio in favor of the child or adolescent patient.

ACCESSION NUMBER: 2004:405481 CAPLUS
DOCUMENT NUMBER: 141:46636
TITLE: Children and adolescents
AUTHOR(S): Bober, J. F.; Preskorn, S. H.
CORPORATE SOURCE: University of Kansas School of Medicine-Wichita, Wichita, KS, 67214-3199, USA
SOURCE: Handbook of Experimental Pharmacology (2004), 157(Antidepressants), 355-378
CODEN: HEPHD2; ISSN: 0171-2004
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The invention relates generally to the enantiomers of p-hydroxymilnacipran or congeners thereof. Biol. assays revealed that racemic p-hydroxymilnacipran is approx. equipotent in inhibiting serotonin and norepinephrine uptake (IC50 = 28.6 nM for norepinephrine, IC50 = 21.7 nM for serotonin). Interestingly, (+)-p-hydroxymilnacipran is a more potent inhibitor of norepinephrine uptake than serotonin uptake (IC50 = 10.3 nM for norepinephrine, IC50 = 22 nM for serotonin). In contrast, (-)-p-hydroxymilnacipran is a more potent inhibitor of serotonin uptake compared to norepinephrine uptake (IC50 = 88.5 nM for norepinephrine, IC50 = 40.3 nM for serotonin). The invention also relates to salts and prodrug forms of the above compds. In certain embodiments, the compds. of the invention and a pharmaceutically acceptable excipient are combined to prepare a formulation for administration to a patient. Finally, the invention relates to methods of treating mammals suffering from various afflictions, e.g., depression, chronic pain, or fibromyalgia, comprising administering to a mammal in need thereof a therapeutically effective amount of a compound of the invention. Compound preparation is included.

ACCESSION NUMBER: 2004:392439 CAPLUS
DOCUMENT NUMBER: 140:400095
TITLE: Stereoisomers of p-hydroxy-milnacipran, and therapeutic use
INVENTOR(S): Rariy, Roman V.; Heffernan, Michael; Buchwald, Stephen L.; Swager, Timothy M.
PATENT ASSIGNEE(S): Collegium Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039320	A2	20040513	WO 2003-US33681	20031022
WO 2004039320	A3	20040624		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004142904	A1	20040722	US 2003-691465	20031022
PRIORITY APPLN. INFO.:			US 2002-421640P P	20021025
			US 2002-423062P P	20021101
			US 2003-445142P P	20030205

OTHER SOURCE(S): MARPAT 140:400095

L9 ANSWER 13 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The invention discloses the use of compds. and composition of compds. that modulate norepinephrine levels for the prevention and treatment of vasomotor symptoms, such as hot flush, caused by, inter alia, thermoregulatory dysfunctions. Compds. of the invention include e.g. desipramine.

ACCESSION NUMBER: 2004:354797 CAPLUS
DOCUMENT NUMBER: 140:350606
TITLE: Use of norepinephrine reuptake modulators for preventing and treating vasomotor symptoms
INVENTOR(S): Deecher, Darlene Coleman; Merchenthaler, Istvan Joseph; Leventhal, Liza; Sipe, Kimberly Jean; O'Connor, Lawrence Thomas
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035058	A1	20040429	WO 2003-US32759	20031015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004152710	A1	20040805	US 2003-685812	20031014
PRIORITY APPLN. INFO.:			US 2002-418591P	P 20021015
			US 2003-685812	A 20031014

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 14 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The invention discloses the use of compds. and compns. of compds. that modulate norepinephrine levels for the treatment of vasomotor symptoms, e.g. thermoregulatory disorders. The invention also discloses the use of compds. and compns. of compds. having norepinephrine reuptake inhibitor (NRI) activity alone or norepinephrine reuptake inhibitor and serotonin reuptake inhibitor (NRI/SRI) dual activity in combination with 5-HT2a receptor antagonist activity.

ACCESSION NUMBER: 2004:354778 CAPLUS
DOCUMENT NUMBER: 140:350603
TITLE: A method of treating vasomotor symptoms using a compound having norepinephrine reuptake inhibitor activity and 5-HT2a antagonistic activity
INVENTOR(S): Deecher, Darlene Coleman; Merchenthaler, Istvan Joseph
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035036	A1	20040429	WO 2003-US32554	20031015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004180879	A1	20040916	US 2003-685974	20031014
PRIORITY APPLN. INFO.:			US 2002-418516P	P 20021015
			US 2003-685974	A 20031014

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 15 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review. Since attention-deficit/hyperactivity disorder (ADHD) is usually diagnosed in children, evidence from the studies of pharmacol. treatments for children with ADHD is used to inform pharmacol. treatment recommendations for adults. A large percentage of children diagnosed with ADHD have symptoms that persist into adolescence and adulthood. Evidence shows that pharmacol. treatments improve functional outcomes in children with ADHD, and studies using similar pharmacol. treatments show pos. results in adults with ADHD. This article reviews the use of long-acting methylphenidate, mixed amphetamine salts, desipramine, monoamine oxidase inhibitors, bupropion, and atomoxetine in studies of children, adolescents, and adults with ADHD.

ACCESSION NUMBER: 2004:345153 CAPLUS
DOCUMENT NUMBER: 140:417062
TITLE: ADHD treatment across the life cycle
AUTHOR(S): Spencer, Thomas J.
CORPORATE SOURCE: Department of Pediatric Psychopharmacology, Massachusetts General Hospital, Department of Psychiatry, Harvard Medical School, Boston, USA
SOURCE: Journal of Clinical Psychiatry (2004), 65(Suppl. 3), 22-26
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 16 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The invention provides novel antipsychotic therapies and compns. useful therein and provides methods for identifying new candidate mols. for the treatment of psychosis based on the proportional binding affinities for α2 adrenergic and D2 dopamine receptors.

ACCESSION NUMBER: 2004:101019 CAPLUS
DOCUMENT NUMBER: 140:157473
TITLE: Antipsychotic combination therapies and compositions of an alpha-2 adrenergic receptor antagonist and an atypical antipsychotic neuroleptic
INVENTOR(S): Pickar, David; Wadenberg, Marie-Louise; Svensson, Torgny
PATENT ASSIGNEE(S): Potomac, Pharma Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004011031	A1	20040205	WO 2003-US23440	20030728
WO 2004011031	C2	20040422		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004127489	A1	20040701	US 2003-629123	20030728
PRIORITY APPLN. INFO.:			US 2002-398718P	P 20020729
			US 2002-398719P	P 20020729
			US 2002-398720P	P 20020729
			US 2002-402542P	P 20020812
			US 2002-433781P	P 20021217
			US 2002-433782P	P 20021217
			US 2002-433785P	P 20021217

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L9 ANSWER 17 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB We present an extension and confirmation of our previously published method for the prediction of volume of distribution (VD) in humans for neutral and basic compds. It is based on two exptl. determined physicochem. parameters, ElogD (7.4) and fi(7.4), the latter being the fraction of compound ionized at pH 7.4, and on the fraction of free drug in plasma (fu). By regressing the fraction unbound in tissues, fut, vs. the above parameters, we demonstrate the ruggedness of the method in predicting VD through the Oie-Tozer equation, via the use of several testing approaches. A comparison is also presented between several methods based on animal pharmacokinetic data, using the same set of proprietary compds., and it lends further support for the use of this method, as opposed to methods that require the gathering of pharmacokinetic data in laboratory animals. The reduction in the use of animals and the overall faster and cheaper accessibility of the parameters used make this method highly attractive for prospectively predicting the VD of new chemical entities in humans.

ACCESSION NUMBER: 2004:85683 CAPLUS
DOCUMENT NUMBER: 140:246128
TITLE: Prediction of Human Volume of Distribution Values for Neutral and Basic Drugs. 2. Extended Data Set and Leave-Class-Out Statistics
AUTHOR(S): Lombardo, Franco; Obach, R. Scott; Shalaeva, Marina Y.; Gao, Feng
CORPORATE SOURCE: Molecular Properties Group, Pharmacokinetics, Dynamics and Metabolism, and Nonclinical Statistics Group, Pfizer Global Research and Development, Groton Laboratories, Groton, CT, 06340, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(5), 1242-1250
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 18 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Disclosed is use of reboxetine in combination with a smoking-cessation enhancing agent for promoting smoking cessation. Also disclosed is a composition comprising reboxetine and a smoking-cessation enhancing agent for use for promoting smoking cessation. Examples of the smoking-cessation enhancing agents include nicotine, an antidepressant, a nicotine receptor antagonist, and an opioid antagonist. Examples of compns. are combinations of reboxetine with bupropion.

ACCESSION NUMBER: 2004:20476 CAPLUS
DOCUMENT NUMBER: 140:53478
TITLE: Method of promoting smoking cessation
INVENTOR(S): Wong, Erik H. F.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002463	A2	20040108	WO 2003-US16232	20030626
WO 2004002463	A3	20040219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004102440	A1	20040527	US 2003-602447	20030624
PRIORITY APPLN. INFO.:			US 2002-392893P	P 20020701

L9 ANSWER 19 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Drugs that affect neurotransmitter release can induce changes in neuroregulation during chronic administration. Thus, in addition to recurrence of symptoms of the illness, discontinuation of treatment can be associated with clin. signs and symptoms related to these changes. Atomoxetine, a new drug approved in the United States for treatment of attention deficit/hyperactivity disorder (ADHD), is associated with blockade of the presynaptic norepinephrine transporter. Because treatment of ADHD typically involves chronic treatment, the potential for production of a discontinuation syndrome as well as recurrence of symptoms upon drug discontinuation were assessed as part of the clin. development process. The effects of discontinuation of atomoxetine were assessed in children and adults with ADHD following 9 to 10 wk of continuous therapy in 4 large studies. Symptoms of ADHD worsened following drug discontinuation but did not return to pretreatment levels. The incidence of discontinuation-emergent adverse events was low and there were no statistically significant differences between the patients abruptly discontinuing from atomoxetine and those continuing on placebo. Discontinuation of atomoxetine did not result in the development of an acute discontinuation syndrome and was well tolerated. It appears that atomoxetine may be discontinued without risk for symptom rebound or discontinuation-emergent adverse effects. Tapering of doses is not necessary when atomoxetine is discontinued.

ACCESSION NUMBER: 2004:13455 CAPLUS
DOCUMENT NUMBER: 141:133903
TITLE: Changes in Symptoms and Adverse Events After Discontinuation of Atomoxetine in Children and Adults With Attention Deficit/Hyperactivity Disorder: A Prospective, Placebo-Controlled Assessment
AUTHOR(S): Wernicke, Joachim F.; Adler, Lenard; Spencer, Thomas; West, Scott A.; Allen, Albert J.; Heiligenstein, John; Milton, Denai; Ruff, Dustin; Brown, W. Jeffrey; Kelsey, Douglas; Michelson, David
CORPORATE SOURCE: Lilly Research Laboratories, Indianapolis, IN, USA
SOURCE: Journal of Clinical Psychopharmacology (2004), 24(1), 30-35
CODEN: JCPYDR; ISSN: 0271-0749
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 20 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The invention provides a method for treating obesity and minimizing metabolic risk factors associated therewith using e.g. zonisamide or other weight loss-promoting anticonvulsants, either alone or in combination with bupropion or other compound that enhances the activity of norepinephrine and/or dopamine via uptake inhibition or other mechanism.

ACCESSION NUMBER: 2003:931170 CAPLUS
DOCUMENT NUMBER: 139:391377
TITLE: Method using anticonvulsant agents and compounds enhancing norepinephrine and/or dopamine activity for treating obesity
INVENTOR(S): Gadde, Kishore M.; Krishnan, K. Ranga R.
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097046	A1	20031127	WO 2003-US15703	20030519
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004033965	A1	20040219	US 2003-440404	20030519
US 2004198668	A1	20041007	US 2004-830071	20040423
PRIORITY APPLN. INFO.:			US 2002-380874P	P 20020517
			US 2003-440404	A1 20030519

OTHER SOURCE(S): MARPAT 139:391377
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Background: Atomoxetine is a highly specific presynaptic inhibitor of the noradrenaline (norepinephrine) transporter that was recently approved in the US for the treatment of patients with attention-deficit/hyperactivity disorder (ADHD). Adverse effects on the cardiovascular system, including abnormalities in heart rate, blood pressure, or cardiac rhythm have been associated with several noradrenergic medications. Objective: To further elucidate the magnitude and impact of blood pressure and pulse elevations in patients taking atomoxetine. Study Design: Short-term cardiovascular safety in children, adolescents, and adults with ADHD was assessed in five randomized, double-blind trials (duration up to 10 wk) with atomoxetine (n = 612) or placebo (n = 474). Long-term cardiovascular safety in children and adolescents (n = 169) was assessed in patients who entered an open-label extension or a blinded continuation following short-term treatment. Methods: Adverse events, blood pressure, sitting pulse, and electrocardiograms (ECGs) were collected throughout the trials. QT intervals were corrected for heart rate by a data-specific correction factor (QTcD; derived from baseline ECGs) as well as standard methods. Results: Atomoxetine treatment was associated with small but statistically significant increases in mean systolic blood pressure in adults and diastolic blood pressure in children and adolescents. Mean pulse rate increased for all atomoxetine treatment groups. The increases in blood pressure and pulse tended to occur early in therapy, stabilized, and returned toward baseline upon drug discontinuation. There was no significant difference between atomoxetine and placebo treatment groups in change in QTcD interval for all study populations. Palpitations in the adult patient population were the only significant cardiovascular adverse event ($p = 0.037$) occurring more frequently in the atomoxetine treatment group (3.7%) than in the placebo group (0.8%). Discontinuations due to cardiovascular-related events were very uncommon in the adult group, and did not occur in the child/adolescent group. Conclusion: White atomoxetine has noradrenergic activity, increases in pulse and blood pressure were small and of little, if any, clin. significance. Atomoxetine was not associated with QT interval prolongation. Cardiovascular effects of atomoxetine were minimal, and atomoxetine was well tolerated in short- and long-term studies.

ACCESSION NUMBER: 2003:715543 CAPLUS
DOCUMENT NUMBER: 139:270924
TITLE: Cardiovascular effects of atomoxetine in children, adolescents, and adults
AUTHOR(S): Wernicke, Joachim F.; Faries, Douglas; Girod, Donald; Brown, Jeffrey W.; Gao, Haitao; Kelsey, Douglas; Quintana, Humberto; Lipetz, Robert; Michelson, David; Heiligenstein, John
CORPORATE SOURCE: Lilly Research Laboratories, Indianapolis, IN, USA
SOURCE: Drug Safety (2003), 26(10), 729-740
CODEN: DRSAEA; ISSN: 0114-5916
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L9 ANSWER 22 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB One of the common neurochem. features of many drugs of abuse is their ability to directly or indirectly enhance dopaminergic activity in the brain, particularly within the ventral tegmental-nucleus accumbens pathway. Dopaminergic pathways in the frontal and limbic cortex also may be targets for these agents, where pharmacol. effects could result in heightened attention and/or support self-administration behavior. The purpose of this study was to determine whether drugs from differing pharmacol. classes that exhibit abuse potential would share the ability to counter distractability in the delayed matching task. Well trained mature macaques performed a computer-assisted delayed matching-to-sample task which included trials associated with three delay intervals and randomly interspersed task-relevant distractors. Drug regimens included four to five doses and subjects were tested no more than twice per wk. All but one of the six compds. (tomoxetine), on average, increased task accuracy for either non-distractor or distractor trials. It was evident that for several compds., doses required to improve accuracy for non-distractor trials were routinely greater than the doses required to improve accuracy for distractor trials. Data for the individualized Best dose (based upon the subject's optimal level of accuracy during distractor trials) revealed statistically significant distractor-related improvements in task accuracy for the same five compds. The relative efficacy for reversing distractor-induced decrements in task accuracy was estimated by the level of improvement with respect to baseline: nomifensine (31%) > nicotine (22%) ≈ morphine (19%) ≈ caffeine (19%) ≈ methylphenidate (22%) > tomoxetine (9%). Tomoxetine (noradrenergic preferring) was the only compound that did not produce a significant improvement in accuracy. These results provide pharmacol. support for the concept that attentional mechanisms may play an important role in the "environmental" associative aspects of drug seeking behavior, and as such they may provide the basis for treatment strategies aimed at preventing relapse in detoxified addicts.

ACCESSION NUMBER: 2003:674569 CAPLUS
DOCUMENT NUMBER: 140:139228
TITLE: Enhanced attention in rhesus monkeys as a common factor for the cognitive effects of drugs with abuse potential
AUTHOR(S): Bain, John N.; Prendergast, Mark A.; Terry, Alvin V.; Arneric, Stephen P.; Smith, Mark A.; Buccafusco, Jerry J.
CORPORATE SOURCE: Department of Pharmacology and Toxicology, Alzheimer's Research Center, Medical College of Georgia, Augusta, GA, 30912-2300, USA
SOURCE: Psychopharmacology (Berlin, Germany) (2003), 169(2), 150-160
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L9 ANSWER 22 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L9 ANSWER 23 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Atomoxetine (Strattera, Eli Lilly & Co.) is a selective noradrenaline reuptake inhibitor that has been studied for use in the treatment of attention-deficit/hyperactivity disorder (ADHD). So far, two open-label and seven randomized, double-blind, placebo-controlled, clin. trials have been published, six in youths and three in adults. Each of these trials has shown a pos. response as measured by the primary efficacy measures, the ADHD-IV Rating Scale (ADHD RS) or the Conners Adult ADHD Rating Scale (CAARS). Atomoxetine has generally been well tolerated. In Nov. of 2002 the FDA approved atomoxetine for use in the US for the treatment of ADHD in children, adolescents and adults. Atomoxetine is the first nonstimulant approved by the FDA for the treatment of ADHD and the first medication approved for the treatment of adult ADHD.

ACCESSION NUMBER: 2003:493353 CAPLUS
DOCUMENT NUMBER: 140:53185
TITLE: Atomoxetine: a selective noradrenaline reuptake inhibitor for the treatment of attention-deficit/hyperactivity disorder
AUTHOR(S): Kratochvil, Christopher J.; Vaughan, Brigette S.; Harrington, Martin J.; Burke, William J.
CORPORATE SOURCE: Department of Psychiatry, University of Nebraska Medical Center, Omaha, 68191-5581, USA
SOURCE: Expert Opinion on Pharmacotherapy (2003), 4(7), 1165-1174
CODEN: EOPHF7; ISSN: 1465-6566
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 24 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Selective norepinephrine reuptake inhibitors, particularly atomoxetine, reboxetine and 2-alkylthio substituted phenoxyphenyl propylamines, are used for the treatment of cognitive failure, including cognitive failure due to dementia, delirium and schizophrenia.

ACCESSION NUMBER: 2003:472376 CAPLUS
DOCUMENT NUMBER: 139:30841
TITLE: Use of norepinephrine reuptake inhibitors for the treatment of cognitive failure
INVENTOR(S): Bymaster, Franklin Porter; Gehlert, Donald Richard; McKinzie, David Lee; Yang, Charles Renkin
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003049724	A1	20030619	WO 2002-US36132	20021127
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
BR 2002013581	A	20040824	BR 2002-13581	20021127
EP 1458368	A1	20040922	EP 2002-789574	20021127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: US 2001-339174P P 20011211
WO 2002-US36132 W 20021127

OTHER SOURCE(S): MARPAT 139:30841
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 25 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Selective norepinephrine reuptake inhibitors, e.g. atomoxetine, are used to treat tic disorders.

ACCESSION NUMBER: 2003:454102 CAPLUS
DOCUMENT NUMBER: 139:974
TITLE: Use of norepinephrine reuptake inhibitors for the treatment of tic disorders
INVENTOR(S): Allen, Albert John; Michelson, David
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003047560	A1	20030612	WO 2002-US33628	20021112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1455770	A1	20040915	EP 2002-784195	20021112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: US 2001-334494P P 20011130
WO 2002-US33628 W 20021112

OTHER SOURCE(S): MARPAT 139:974
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 26 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A process for producing an optically active amino alc. is provided that includes a step in which a nitro ketone or a cyano ketone is reacted with a hydrogen-donating organic or inorg. compound in the presence of a transition metal compound catalyst having an optically active nitrogen-containing compound as an asym. ligand to give an optically active nitro alc. or an optically active cyano alc., and a step in which the above optically active alc. is further reduced to efficiently produce an optically active amino alc. Thus, PhCOCH2CN was reduced with HCO2H in presence of Et3N and chloro[(S,S)-N-(p-toluenesulfonyl)-1,2-diphenylethylenediamine](p-cymene)ruthenium to give (S)-HOCHPhCH2CN in 98% ee. This compound was reduced with BH3.Me2S to give (S)-HOCHPhCH2CH2NH2 with 98% ee. The alcs. are intermediates for pharmaceuticals, such as fluoxetine, tomoxetine, nisoxetine and norfluoxetine.

ACCESSION NUMBER: 2003:356091 CAPLUS
DOCUMENT NUMBER: 138:353733
TITLE: Process for producing optically active amino alcohols
INVENTOR(S): Watanabe, Masahito; Murata, Kunihiko; Ikariya, Takao
PATENT ASSIGNEE(S): Kanto Kagaku Kabushiki Kaisha, Japan
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1308435	A2	20030507	EP 2002-24517	20021030
EP 1308435	A3	20030604		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2003201269	A2	20030718	JP 2002-251994	20020829
JP 3504254	B2	20040308		
CA 2409906	AA	20030430	CA 2002-2409906	20021028
JP 2003201270	A2	20030718	JP 2002-316217	20021030
US 2003171592	A1	20030911	US 2002-285164	20021031
US 6686505	B2	20040203		

PRIORITY APPLN. INFO.: JP 2001-335322 A 20011031
JP 2002-251994 A 20020829

OTHER SOURCE(S): MARPAT 138:353733

L9 ANSWER 27 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Buccal aerosol sprays or capsules using polar and non-polar solvent have now been developed which provide biol. active compds. for rapid absorption through the oral mucosa, resulting in fast onset of effect. The buccal polar compns. of the invention comprise formulation A: aqueous polar solvent, active compound, and optional flavoring agent; formulation B: aqueous polar solvent, active compound, optionally flavoring agent, and propellant; formulation C: non-polar solvent, active compound, and optional flavoring agent; and formulation D: non-polar solvent, active compound, optional flavoring agent, and propellant. Thus, a lingual spray contained sumatriptan succinate 10-15, EtOH 10-20, propylene glycol 10-15, PEG 35-40, water 10-15, and flavors 2-3%.

ACCESSION NUMBER: 2003:319255 CAPLUS
DOCUMENT NUMBER: 138:343854
TITLE: Buccal sprays or capsules containing drugs for treating disorders of the central nervous system
INVENTOR(S): Dugger, Harry A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. Ser. No. 537,118.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003077227	A1	20030424	US 2002-230060	20020829
WO 9916417	A1	19990408	WO 1997-US17899	19971001
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 1029536	A1	20000823	EP 2000-109347	19971001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1036561	A1	20000920	EP 2000-109357	19971001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2004035021	A2	20040429	WO 2003-US26847	20030827
WO 2004035021	A3	20041111		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004141923	A1	20040722	US 2003-671720	20030929

L9 ANSWER 27 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 2004120895	A1	20040624	US 2003-726585	20031204
PRIORITY APPLN. INFO.:			WO 1997-US17899	A2 19971001
			US 2000-537118	A2 20000329
			EP 1997-911621	A3 19971001
			US 2002-230060	A 20020829

L9 ANSWER 28 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The invention discloses the use of inhibitors of the noradrenaline reuptake system for the production of a medicament for the treatment of motor inefficiency or increasing the efficiency of motor learning.

ACCESSION NUMBER: 2003:279592 CAPLUS
DOCUMENT NUMBER: 138:265676
TITLE: Noradrenaline reuptake inhibitors for increasing the effectiveness of motor learning
INVENTOR(S): Gerloff, Christian; Plewnia, Christian
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 4 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10244537	A1	20030410	DE 2002-10244537	20020925
PRIORITY APPLN. INFO.:			DE 2001-10147383	IA 20010926

L9 ANSWER 29 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A pharmaceutical composition comprising a polypeptide and an active agent attached to said polypeptide is disclosed.

ACCESSION NUMBER: 2003:202410 CAPLUS
DOCUMENT NUMBER: 138:226705
TITLE: Novel pharmaceuticals comprising drug conjugates with polypeptide carriers
INVENTOR(S): Picariello, Thomas
PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 2059 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020200	A2	20030313	WO 2001-US43117	20011116
WO 2003020200	A3	20030912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1357928	A2	20031105	EP 2001-273387	20011116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 2000-248600P	P 20001116
			US 2000-248601P	P 20001116
			US 2000-248603P	P 20001116
			US 2000-248604P	P 20001116
			US 2000-248606P	P 20001116
			US 2000-248607P	P 20001116
			US 2000-248608P	P 20001116
			US 2000-248609P	P 20001116
			US 2000-248611P	P 20001116
			US 2000-248689P	P 20001116
			US 2000-248691P	P 20001116
			US 2000-248692P	P 20001116
			US 2000-248693P	P 20001116
			US 2000-248694P	P 20001116

L9 ANSWER 29 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 2000-248695P	P	20001116
US 2000-248696P	P	20001116
US 2000-248697P	P	20001116
US 2000-248698P	P	20001116
US 2000-248701P	P	20001116
US 2000-248702P	P	20001116
US 2000-248703P	P	20001116
US 2000-248704P	P	20001116
US 2000-248705P	P	20001116
US 2000-248706P	P	20001116
US 2000-248707P	P	20001116
US 2000-248708P	P	20001116
US 2000-248709P	P	20001116
US 2000-248710P	P	20001116
US 2000-248711P	P	20001116
US 2000-248712P	P	20001116
US 2001-248664P	P	20011116
US 2001-248665P	P	20011116
US 2001-248666P	P	20011116
US 2001-248667P	P	20011116
US 2001-248668P	P	20011116
US 2001-248669P	P	20011116
US 2001-248671P	P	20011116
US 2001-248672P	P	20011116
US 2001-248673P	P	20011116
US 2001-248674P	P	20011116
US 2001-248675P	P	20011116
US 2001-248676P	P	20011116
US 2001-248677P	P	20011116
US 2001-248678P	P	20011116

L9 ANSWER 29 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 2001-248679P	P	20011116
US 2001-248680P	P	20011116
US 2001-248681P	P	20011116
US 2001-248682P	P	20011116
US 2001-248683P	P	20011116
US 2001-248684P	P	20011116
US 2001-248765P	P	20011116
US 2001-248766P	P	20011116
US 2001-248767P	P	20011116
US 2001-248773P	P	20011116
US 2001-248774P	P	20011116
US 2001-248775P	P	20011116
US 2001-248778P	P	20011116
US 2001-248780P	P	20011116
US 2001-248781P	P	20011116
US 2001-248783P	P	20011116
US 2001-248784P	P	20011116
US 2001-248785P	P	20011116
US 2001-248786P	P	20011116
US 2001-248787P	P	20011116
US 2001-248790P	P	20011116
US 2001-248791P	P	20011116
US 2001-248792P	P	20011116
US 2001-248793P	P	20011116
US 2001-248833P	P	20011116
US 2001-248848P	P	20011116
US 2001-248849P	P	20011116
WO 2001-US43117	W	20011116

L9 ANSWER 30 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review. Atomoxetine, a norepinephrine reuptake inhibitor, is the first nonstimulant agent approved for the treatment of ADHD. It has been approved for use in pediatric and adult patients. Atomoxetine improves ADHD symptom severity vs. placebo, as evaluated by the ADHD Rating Scale (ADHD RS), and its efficacy appears comparable to immediate-release (IR) methylphenidate. Atomoxetine requires dosage titration and may be administered once or twice daily. Common side effects seen in both pediatric and adult patients include nausea, decreased appetite, and dizziness. Dosage adjustments are necessary for patients receiving atomoxetine and cytochrome P 450 2D6 inhibitors. Based on average wholesale price (AWP), atomoxetine is more costly than existing ADHD therapies. Atomoxetine provides an alternative ADHD therapy for patients who may fail or cannot tolerate conventional treatments.

ACCESSION NUMBER: 2003:177424 CAPLUS
DOCUMENT NUMBER: 138:348232
TITLE: A nonstimulant therapeutic option for children and adults with attention-deficit hyperactivity disorder
AUTHOR(S): Baldinger, Sandra L.; Yogman, Michael W.
CORPORATE SOURCE: Provider Service Network, Boston, MA, USA
SOURCE: Formulary (2003), 38(2), 85-86,92,95-100
CODEN: FORMF9; ISSN: 1082-801X
PUBLISHER: Advanstar Communications, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 31 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review. There has been substantial development of pharmacol. treatments for attention-deficit hyperactivity disorder (ADHD) recently. The greatest change is the approval of new delivery systems for methylphenidate (MPH) and amphetamine (AMP) that permit once a day dosing. There are also a number of new compds. under development for the disorder, including several non-stimulant agents. These compds. target the noradrenergic, histaminergic and dopaminergic systems. The recent developments in the pharmacol. treatment of ADHD should increase therapeutic options and the percentage of individuals with the disorder who can be effectively treated.

ACCESSION NUMBER: 2003:157384 CAPLUS
DOCUMENT NUMBER: 139:254495
TITLE: Drugs under investigation for attention-deficit hyperactivity disorder
AUTHOR(S): Schweitzer, Julie B.; Holcomb, Henry H.
CORPORATE SOURCE: Maryland Psychiatric Research Center, University of Maryland School of Medicine, Baltimore, MD, 21228, USA
SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2002), 3(8), 1207-1211
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 32 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A method for prevention and/or treatment of ADHD in a patient in need thereof, the method comprising administering to the patient an effective amount of 2-amino-4,5,6,7-tetrahydro-6-n-propylaminobenzothiazole or a pharmacol. acceptable acid addition salt, hydrate, or solvate thereof.

ACCESSION NUMBER: 2003:133945 CAPLUS
DOCUMENT NUMBER: 138:163585
TITLE: Pramipexole for the treatment of ADHD
INVENTOR(S): Reess, Juergen; Borsini, Franco
PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma Kg, Germany
SOURCE: U.S. Pat. Appl. Publ., 5 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003036555	A1	20030220	US 2002-198480	20020718
DE 10137633	A1	20030220	DE 2001-10137633	20010803
WO 2003013520	A1	20030220	WO 2002-EP8500	20020731
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1416930	A1	20040512	EP 2002-762417	20020731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: DE 2001-10137633 A 20010803
US 2001-312241P P 20010814
WO 2002-EP8500 W 20020731

L9 ANSWER 33 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The present invention relates to materials and methods for treating neurol. diseases and disorders including but not limited to epilepsy and autism, as well as general cognitive problems. Preferred compds. include carnosine and homocarnosine and N-acetyl, methylated (anserine, ophidine), decarboxylated (carcinine) and tauryl derivs. of carnosine and homocarnosine.

ACCESSION NUMBER: 2003:133030 CAPLUS
DOCUMENT NUMBER: 138:163577
TITLE: Improving neurological functions
INVENTOR(S): Chez, Michael G.
PATENT ASSIGNEE(S): Carn-Aware LLC, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013514	A1	20030220	WO 2002-US22341	20020715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2001-310710P P 20010808
US 2001-325136P P 20010927

OTHER SOURCE(S): MARPAT 138:163577
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 34 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The invention provides improved formulations and methods for the treatment of neurol. disorders. A method is described for decreasing inter-individual variability due to CYP2D6-mediated metabolism in the inhibition of norepinephrine uptake by administering to a human that is a CYP2D6 extensive metabolizer an effective amount of atomoxetine in combination with an inhibitor of CYP2D6.

ACCESSION NUMBER: 2003:133010 CAPLUS
DOCUMENT NUMBER: 138:163575
TITLE: Combination therapy for the treatment of neurological disorders
INVENTOR(S): Allen, Albert John; Michelson, David; Sauer, John-Michael; Witcher, Jennifer Wright
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003013492	A1	20030220	WO 2002-US21294	20020726
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1423104	A1	20040602	EP 2002-756386	20020726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004176466	A1	20040909	US 2004-484646	20040122

PRIORITY APPLN. INFO.: US 2001-310981P P 20010808
WO 2002-US21294 W 20020726

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 35 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Atomoxetine is a nonstimulant drug being studied for the treatment of attention-deficit/hyperactivity disorder (ADHD). Atomoxetine is a highly specific inhibitor of the presynaptic norepinephrine transporter with minimal affinity for other noradrenergic receptors or other neurotransmitter transporters or receptors. Results of 2 proof-of-concept studies are reported that tested the hypothesis that a selective inhibitor of presynaptic norepinephrine uptake would be effective for the treatment of ADHD in school-aged children. Two identical 12-wk, stratified, randomized, double-blind, placebo-controlled trials were conducted in children who met DSM-IV criteria for ADHD. The primary efficacy outcome measure was the mean change from baseline to endpoint in the Attention-Deficit/Hyperactivity Disorder Rating Scale (ADHD RS) total score. Secondary efficacy measures included the Clin. Global Impressions-ADHD-Severity (CGI-ADHD-S) and the Conners' Parent Rating Scale-Revised: Short Form (CPRS-R:S). A total of 291 patients were randomized in the 2 trials combined (Study 1, N = 147; Study 2, N = 144). Stimulant-naive patients were randomized to atomoxetine, placebo, or methylphenidate. Patients with prior stimulant exposure were randomized to atomoxetine or placebo. Atomoxetine significantly reduced ADHD RS total scores compared with placebo in each study ($p < .001$). Changes in the CGI-ADHD-S (Study 1: $p = .003$; Study 2: $p = .001$) and CPRS-ADHD Index (Study 1: $p = .023$; Study 2: $p < .001$) also showed atomoxetine to be statistically significantly superior to placebo in reducing ADHD symptoms. Atomoxetine was found to be well tolerated in this population of pediatric patients. Two studies of atomoxetine early in its development confirmed that atomoxetine, a specific and selective inhibitor of noradrenergic uptake, was effective for the treatment of children with ADHD. In addition, atomoxetine was found to be well tolerated.

ACCESSION NUMBER: 2003:90776 CAPLUS
DOCUMENT NUMBER: 138:180579
TITLE: Results from 2 proof-of-concept, placebo-controlled studies of atomoxetine in children with attention-deficit/hyperactivity disorder
AUTHOR(S): Spencer, Thomas; Heiligenstein, John H.; Biederman, Joseph; Faries, Douglas E.; Kratochvil, Christopher J.; Conners, C. Keith; Potter, William Z.
CORPORATE SOURCE: Massachusetts General Hospital, Boston, USA
SOURCE: Journal of Clinical Psychiatry (2002), 63(12), 1140-1147
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 36 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Background: Attention-deficit/hyperactivity disorder (ADHD) has been less studied in adults than in children, and the treatment studies reported to date have been small, single-center trials. To assess the efficacy of atomoxetine, a new and highly selective inhibitor of the norepinephrine transporter, we conducted two large, multicenter treatment trials. Methods: Two identical studies using randomized, double-blind, placebo-controlled designs and a 10-wk treatment period were conducted in adults with DSM-IV-defined ADHD as assessed by clin. history and confirmed by a structured interview (study I, n = 280; study II, n = 256). The primary outcome measure was a comparison of atomoxetine and placebo using repeated measures mixed model anal. of postbaseline values of the Conners' Adult ADHD Rating Scale. Results: In each study, atomoxetine was statistically superior to placebo in reducing both inattentive and hyperactive and impulsive symptoms as assessed by primary and secondary measures. Discontinuations for adverse events among atomoxetine patients were under 10% in both studies. Conclusions: Atomoxetine appears to be an efficacious treatment for adult ADHD. Its lack of abuse potential may be an advantage for many patients.

ACCESSION NUMBER: 2003:53172 CAPLUS
DOCUMENT NUMBER: 139:240117
TITLE: Atomoxetine in adults with ADHD: two randomized, placebo-controlled studies
AUTHOR(S): Michelson, David; Adler, Lenard; Spencer, Thomas; Reimherr, Frederick W.; West, Scott A.; Allen, Albert J.; Kelsey, Douglas; Wernicke, Joachim; Dietrich, Anthony; Milton, Denai
CORPORATE SOURCE: Lilly Research Laboratories, Indianapolis, IN, USA
SOURCE: Biological Psychiatry (2003), 53(2), 112-120
CODEN: BIPCBF; ISSN: 0006-3223
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 37 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review. Atomoxetine is a selective norepinephrine reuptake inhibitor that is being developed for the treatment of attention-deficit/hyperactivity disorder (ADHD). Atomoxetine will be the first nonstimulant medication approved by the U.S. Food and Drug Administration (FDA) for the treatment of ADHD. Throughout the testing phases, more than 2000 children and adolescents have been exposed to atomoxetine in clin. trials, with both the number of exposures and the length of exposure time increasing. Serious adverse events have not been clearly associated with the drug, and there have been few discontinuations due to adverse events. The most common drug-related event reported in trials has been decreased appetite and an initial period of weight loss followed by an apparently normal rate of weight gain. These events tend to appear early in the course of treatment with atomoxetine and then decline. Atomoxetine has also been associated with mild increases in blood pressure and pulse that plateau during treatment and resolve upon discontinuation. There have been no effects seen on the QT interval, and the cytochrome P 450 2D6 metabolism of patients seems to have little effect on safety or tolerability of the drug. This article will review the data from completed and ongoing clin. trials available at the time the New Drug Application was submitted to the FDA. Described are serious adverse events, discontinuations, and treatment-emergent adverse events. Specifically, cardiac effects and effects on weight, height, and metabolism that are related to treatment of ADHD with atomoxetine in children and adolescents are discussed.

ACCESSION NUMBER: 2003:2271 CAPLUS
DOCUMENT NUMBER: 138:49290
TITLE: Safety profile of atomoxetine in the treatment of children and adolescents with ADHD
AUTHOR(S): Wernicke, J. F.; Kratochvil, Christopher J.
CORPORATE SOURCE: Eli Lilly and Company, Indianapolis, IN, USA
SOURCE: Journal of Clinical Psychiatry (2002), 63(Suppl. 12), 50-55
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 38 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review. Optimal medications for children with attention-deficit/hyperactivity disorder (ADHD) would be effective, well tolerated, and long acting and not cause mood swings or worsen comorbid conditions. Current medications work on brain dopamine and/or norepinephrine systems, which are thought to be involved in ADHD. The medication class with the most evidence of efficacy in ADHD is stimulants, but they may be abused, are effective for only 4 to 12 h, and may cause mood swings or increase tic severity. In recent years, alternative treatments have been explored.
Tricyclic antidepressants have efficacy comparable to that of stimulants but may cause constipation, dry mouth, tremors, blood pressure changes, and potentially serious side effects including cardiac conduction and repolarization delays. Monoamine oxidase inhibitors may improve ADHD symptoms but are associated with severe dietary restrictions. Serotonin reuptake inhibitors have little or no effect in ADHD but may improve comorbid depression. Bupropion, although less effective than stimulants, may improve both ADHD symptoms and comorbid depression. Antihypertensive agents may improve impulsivity, hyperactivity, and comorbid tics but cause sedation or rebound hypertension. Atomoxetine, which is being developed for ADHD, reduces symptoms of ADHD without exacerbating comorbid conditions and is associated with only minor side effects, including subtle changes in blood pressure and heart rate. Before prescribing a treatment, physicians should consider the appropriateness and effectiveness of any medication for children with ADHD, who may be less tolerant of side effects and less able to monitor and express concerns about their well-being than adults.

ACCESSION NUMBER: 2003:2270 CAPLUS
DOCUMENT NUMBER: 138:49289
TITLE: Novel treatments for attention-deficit/hyperactivity disorder in children
AUTHOR(S): Spencer, Thomas J.; Biederman, Joseph; Wilens, Timothy E.; Faraone, Stephen V.
CORPORATE SOURCE: Pediatric Psychopharmacology Unit, Department of Psychiatry, Harvard Medical School, Psychiatry Service Massachusetts General Hospital, Boston, USA
SOURCE: Journal of Clinical Psychiatry (2002), 63(Suppl. 12), 16-22
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 39 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The purpose of this study was to characterize the effect of potent CYP2D6 inhibition by paroxetine on atomoxetine disposition in extensive metabolizers. This was a single-blind, two-period, sequential study in 22 healthy individuals. In period 1, 20 mg atomoxetine bid was administered to steady state. In period 2, 20 mg paroxetine was administered qd for 17 days. On days 12 through 17, 20 mg atomoxetine bid were coadministered. Plasma pharmacokinetics of atomoxetine, 4-hydroxyatomoxetine, and N-desmethylatomoxetine was determined at steady state in each treatment period. Plasma pharmacokinetics of paroxetine were determined after the 11th and 17th doses. Paroxetine increased Css,max, AUC0-12, and t1/2 of atomoxetine by approx. 3.5-, 6.5-, and 2.5 fold, resp. After coadministration with paroxetine, increases in N-desmethylatomoxetine and decreases in 4-hydroxyatomoxetine concns. were observed No changes in paroxetine pharmacokinetics were observed after coadministration with atomoxetine. It was concluded that inhibition of CYP2D6 by paroxetine markedly affected atomoxetine disposition, resulting in pharmacokinetics similar to poor metabolizers of CYP2D6 substrates.

ACCESSION NUMBER: 2002:884652 CAPLUS
DOCUMENT NUMBER: 139:46424
TITLE: Effect of potent CYP2D6 inhibition by paroxetine on atomoxetine pharmacokinetics
AUTHOR(S): Belle, Donna J.; Ernest, C. Steven; Sauer, John-Michael; Smith, Brian P.; Thomasson, Holly R.; Witcher, Jennifer W.
CORPORATE SOURCE: Departments of Clinical Pharmacology, Drug Disposition, and Global Pharmacokinetics/Pharmacodynamics, Eli Lilly and Company, Indianapolis, IN, USA
SOURCE: Journal of Clinical Pharmacology (2002), 42(11), 1219-1227
CODEN: JCPCBR; ISSN: 0091-2700
PUBLISHER: Sage Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 40 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The selective norepinephrine (NE) transporter inhibitor atomoxetine (formerly called tomoxetine or LY139603) has been shown to alleviate symptoms in Attention Deficit/Hyperactivity Disorder (ADHD). We investigated the mechanism of action of atomoxetine in ADHD by evaluatins the interaction of atomoxetine with monoamine transporters the effects on extracellular levels of monoamines, and the expression of the neuronal activity marker Fos in brain regions. Atomoxetine inhibited binding of radioligands to clonal cell lines transfected with human NE, serotonin (5-HT) and dopamine (DA) transporters with dissociation consts. (Ki) values of 5, 77 and 1451 nM, resp., demonstrating selectivity for NE transporters. In microdialysis studies, atomoxetine increased extracellular (EX) levels of NE in prefrontal cortex (PFC) 3-fold, but did not alter 5-HTEX levels. Atomoxetine also increased DAEX concns. in PFC 3-fold, but did not alter DAEX in striatum or nucleus accumbens. In contrast, the psychostimulant methylphenidate, which is used in ADHD therapy, increased NEEX and DAEX equally in PFC, but also increased DAEX in the striatum and nucleus accumbens to the same level. The expression of the neuronal activity marker Fos was increased 3.7-fold in PFC by atomoxetine administration, but was not increased in the striatum or nucleus accumbens, consistent with the regional distribution of increased DAEX. We hypothesize that the atomoxetine-induced increase of catecholamines in PFC, a region involved in attention and memory, mediates the therapeutic effects of atomoxetine in ADHD. In contrast to methylphenidate, atomoxetine did not increase DA in striatum or nucleus accumbens, suggesting it would not have motoric or drug abuse liabilities.

ACCESSION NUMBER: 2002:878171 CAPLUS
DOCUMENT NUMBER: 139:750
TITLE: Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of rat: a potential mechanism for efficacy in Attention Deficit/Hyperactivity Disorder
AUTHOR(S): Bymaster, Frank P.; Katner, Jason S.; Nelson, David L.; Hemrick-Luecke, Susan K.; Threlkeld, Penny G.; Heiligenstein, John H.; Morin, S. Michelle; Gehlert, Donald R.; Perry, Kenneth W.
CORPORATE SOURCE: Neuroscience Research Division, Lilly Research Laboratories, Indianapolis, IN, USA
SOURCE: Neuropsychopharmacology (2002), 27(5), 699-711
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 41 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Methods for treating an individual with a psychiatric order with a pharmacol. agent that enhances learning or conditioning in combination with a session of psychotherapy are provided. These methods of the invention encompass a variety of methods of psychotherapy, and psychodynamically oriented psychotherapy, and psychiatric orders including fear and anxiety disorders, addictive disorders, addictive disorders including substance-abuse disorders, and mood disorders. The pharmacol. agents used for the methods of the present invention are ones that generally enhance learning or conditioning, including those that increase the level of norepinephrine in the brain, those that increase the level of acetylcholine in the brain, and those that enhance N-methyl-D-aspartate (NMDA) receptor transmission in the brain.

ACCESSION NUMBER: 2002:777652 CAPLUS
DOCUMENT NUMBER: 137:273226
TITLE: Acute pharmacologic augmentation of psychotherapy with enhancers of learning or conditioning
INVENTOR(S): Davis, Michael; Lu, Kwok-Tung; Ressler, Kerry J.
PATENT ASSIGNEE(S): Emory University, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002078629	A2	20021010	WO 2002-US9467	20020328
WO 2002078629	A3	20021128		
W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, T2, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2442330	AA	20021010	CA 2002-2442330	20020328
EP 1383465	A2	20040128	EP 2002-739111	20020328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004530666	T2	20041007	JP 2002-576897	20020328
US 2004208923	A1	20041021	US 2004-473640	20040422

PRIORITY APPLN. INFO.:
US 2001-279868P P 20010329
US 2002-363991P P 20020313
WO 2002-US9467 W 20020328

L9 ANSWER 42 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

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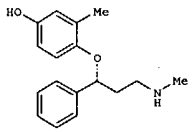


I

AB Pharmaceutically acceptable salts of the monoamine uptake inhibitor, (R)-(-)-N-methyl-3-[(2-methyl-4-hydroxyphenyl)oxy]-3-phenyl-1-aminopropane (I), were prepared For example, (S)-3-chloro-1-phenylpropanol was condensed with 4-[(tert-butoxycarbonyl)oxy]-2-methylphenol in the presence of PPh3 and diisopropylazadicarboxylate in THF to give the aryl ether (85%). Iodination with NaI in 2-butanone (91%), followed by amination with MeNH2 and treatment with 0.1N HCl, afforded I•HCl (55%). The latter inhibited uptake of both serotonin (Ki = 43 nM) and norepinephrine (Ki = 3.0 nM). An open-label study performed on seven healthy men demonstrated that the primary metabolite of (R)-(-)-N-methyl-3-[(2-methylphenyl)oxy]-3-phenyl-1-aminopropane•HCl (II) in both extensive metabolizers (EM) and poor metabolizers (PM) of CYP2D6 substrates is I. The EM subjects metabolized 86.5% of II, while the PM subjects metabolized 40% of II. Formulations of II for treatment of neurol. disorders (no data) are also disclosed.

ACCESSION NUMBER: 2002:695931 CAPLUS
DOCUMENT NUMBER: 137:216750
TITLE: Preparation of 3-aryloxy-3-phenyl-1-aminopropanes as monoamine uptake inhibitors for treatment of neurological disorders
INVENTOR(S): Mattiuz, Edward Louis; Sauer, John-Michael; Wheeler, William Joe; Wong, David Taiwai
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070457	A1	20020912	WO 2002-US3385	20020220
WO 2002070457	C1	20040603		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

L9 ANSWER 42 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2440161	AA	20020912	CA 2002-2440161	20020220
LU 91038	A1	20030911	LU 2002-91038	20020220
GB 2389851	A1	20031224	GB 2003-23169	20020220
EP 1379492	A1	20040114	EP 2002-713538	20020220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300419	A	20040216	EE 2003-419	20020220
ES 2201942	A1	20040316	ES 2003-50052	20020220
BR 2002007716	A	20040323	BR 2002-7716	20020220
JP 2004525912	T2	20040826	JP 2002-569778	20020220
LT 5143	B	20040625	LT 2003-75	20030811
US 2004082666	A1	20040429	US 2003-468553	20030821
FI 2003001191	A	20030825	FI 2003-1191	20030825
SE 2003002361	A	20030903	SE 2003-2361	20030903
NO 2003003921	A	20031105	NO 2003-3921	20030904
DK 200301267	A5	20031106	DK 2003-1267	20030904

PRIORITY APPLN. INFO.:
US 2001-273730P P 20010306
WO 2002-US3385 W 20020220

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 43 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review. Eli Lilly is developing Tomoxetine, a norepinephrine reuptake inhibitor, for the potential treatment of attention deficit hyperactivity disorder (ADHD) and depression. As of May 2000, Tomoxetine was undergoing phase III trials in the US [368128]. An NDA was filed with the FDA in Oct. 2001, with a launch expected in the second half of 2002 [426786]. Tomoxetine was first investigated by Lilly in the 1980s as a potential treatment for depressive illness. The compound was selected from a series of potent inhibitors of norepinephrine reuptake, and reached large-scale phase II clin. trials for depression in 1990. Development for this indication appeared to stop at that time, despite some evidence that Tomoxetine was fairly effective [273943]. In 1996, Lilly apparently restarted preclin. development of Tomoxetine as a potential therapy for ADHD, and submitted EP-00721777 claiming Tomoxetine's utility for this disorder in July of that year [273956]. In June 2001, ABN AMRO predicted sales of $121 million in 2002, rising to $4064 million in 2012 [422762]. In Oct. 2001, analysts at Salomon Smith Barney predicted that the product would make sales of $24 million in 2002, rising to $305 million in 2005 [427501].

ACCESSION NUMBER: 2002:621921 CAPLUS
DOCUMENT NUMBER: 138:180005
TITLE: Tomoxetine (Eli Lilly & Co)
AUTHOR(S): Preti, Antonio
CORPORATE SOURCE: Genneruxi Medical Center, Cagliari, I-09129, Italy
SOURCE: Current Opinion in Investigational Drugs (PharmaPress Ltd.) (2002), 3(2), 272-277
CODEN: COIDAZ; ISSN: 1472-4472
PUBLISHER: PharmaPress Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 44 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

ACCESSION NUMBER: 2002:556104 CAPLUS
DOCUMENT NUMBER: 137:109489
TITLE: Compositions comprising a polypeptide and an active agent
INVENTOR(S): Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randal J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002099013	A1	20020725	US 2001-933708		20010822
US 2004087483	A1	20040506	US 2002-136433		20020502
PRIORITY APPLN. INFO.:			US 2000-247556P	P	20001114
			US 2000-247558P	P	20001114
			US 2000-247559P	P	20001114
			US 2000-247560P	P	20001114
			US 2000-247561P	P	20001114
			US 2000-247594P	P	20001114
			US 2000-247595P	P	20001114
			US 2000-247606P	P	20001114
			US 2000-247607P	P	20001114
			US 2000-247608P	P	20001114
			US 2000-247609P	P	20001114
			US 2000-247610P	P	20001114
			US 2000-247611P	P	20001114
			US 2000-247612P	P	20001114
			US 2000-247620P	P	20001114
			US 2000-247621P	P	20001114
			US 2000-247634P	P	20001114

L9 ANSWER 44 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 2000-247635P	P	20001114
US 2000-247698P	P	20001114
US 2000-247699P	P	20001114
US 2000-247700P	P	20001114
US 2000-247701P	P	20001114
US 2000-247702P	P	20001114
US 2000-247797P	P	20001114
US 2000-247798P	P	20001114
US 2000-247799P	P	20001114
US 2000-247800P	P	20001114
US 2000-247801P	P	20001114
US 2000-247802P	P	20001114
US 2000-247803P	P	20001114
US 2000-247804P	P	20001114
US 2000-247805P	P	20001114
US 2000-247807P	P	20001114
US 2000-247832P	P	20001114
US 2000-247833P	P	20001114
US 2000-247926P	P	20001114
US 2000-247927P	P	20001114
US 2000-247928P	P	20001114
US 2000-247929P	P	20001114
US 2000-247930P	P	20001114
US 2000-642820	A2	20000822
US 2000-248607P	P	20001116
US 2001-933708	A2	20010822

L9 ANSWER 45 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB This invention relates to a chemoenzymic process for the stereoselective preparation of both (R) and (S) enantiomers of 3-hydroxy-3-phenylpropanenitrile, useful as a key intermediate for synthesis of (S)-fluoxetine, (R)-tomoxetine and cognant compds., which comprises reacting cyanohydrin with an acetylating agent in the presence of lipase in an organic solvent, followed by separation of (R)-acetate and (S) alc., hydrolyzing (R)-acetate in the presence of potassium carbonate and methanol, filtering the reaction mixture and evaporating the solvent to obtain the (R) alc.

ACCESSION NUMBER: 2002:555676 CAPLUS
DOCUMENT NUMBER: 137:108394
TITLE: Stereoselective preparation of 3-hydroxy-3-phenylpropionitrile
INVENTOR(S): Kamal, Ahmed; Khanna, Gollapalli Bhasker; Rao, Maddamsetty Venkate; Raghavan, Kondapuram Vijaya
PATENT ASSIGNEE(S): Council of Scientific and Industrial Research, India
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002057475	A1	20020725	WO 2001-IN8		20010122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
GB 2387597	A1	20031022	GB 2003-17492		20010122
GB 2387597	B2	20041110			
JP 2004520039	T2	20040708	JP 2002-558527		20010122
PRIORITY APPLN. INFO.:			WO 2001-IN8	W	20010122

OTHER SOURCE(S): CASREACT 137:108394
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 46 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB Nondependent light drug users received placebo, atomoxetine (20, 45 and 90
mg) or methylphenidate (20 and 40 mg) in a double-blind, Latin square design. Subjective drug effects were assessed by the Visual Analog Scales
(VAS), the Addiction Research Center Inventory (ARCI) and Adjective Rating
Scales (ARS). Psychomotor performance was evaluated by the Digit Symbol Substitution Test (DSST). Physiol. measures were also collected throughout the sessions. Assessments were conducted before and 30, 60, 90, 120, 150, 180 and 240 min after drug administration. Forty milligrams
methylphenidate produced increases in the stimulant portions of the VAS and ARS and the benzedrine, amphetamine, morphine-benzedrine and lysergic acid diethylamide (LSD) subscales of the ARCI relative to placebo. Ninety
mg atomoxetine was reported to be unpleasurable relative to placebo, as indicated by significant increases of the 'bad' and 'sick' portions of the
VAS and the LSD subscale of the ARCI. Compared with placebo, both methylphenidate doses increased systolic blood pressure (BP) and heart rate (HR). For atomoxetine, 90 mg increased diastolic BP, 45 and 90 mg increased systolic BP, and all three doses increased HR relative to placebo. Neither compound produced significant differences from placebo on
DSST performance. These results suggest that atomoxetine does not induce subjective effects similar to those of methylphenidate and suggest that it
is unlikely that atomoxetine will have abuse liability.
ACCESSION NUMBER: 2002:498844 CAPLUS
DOCUMENT NUMBER: 138:215131
TITLE: Comparison of the subjective, physiological, and psychomotor effects of atomoxetine and methylphenidate
in light drug users
AUTHOR(S): Heil, S. H.; Holmes, H. W.; Bickel, W. K.; Higgins, S.
T.; Badger, G. J.; Laws, H. F.; Faries, D. E.
CORPORATE SOURCE: Department of Psychiatry, University of Vermont, Burlington, VT, 05401, USA
SOURCE: Drug and Alcohol Dependence (2002), 67(2), 149-156
CODEN: DADEDV; ISSN: 0376-8716
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 47 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB The present invention relates to methods for the treatment of diseases associated with hyper-proliferation of cells by administering to a subject in
need a therapeutically effective amount of at least one psychotropic agent.
Specific proliferative diseases against which psychotropic agents were found to be effective are cancer, including multi-drug resistant cancer and diseases associated with hyper-proliferation of the skin cells, such as
psoriasis and hyperkeratosis. Among the examples provided is one demonstrating the effectiveness of topical administration of thioridazine cream on psoriasis in a couple of patients. The effectiveness of psychotropics in inhibiting proliferation of cancer cells and in sensitizing doxorubicin cytotoxicity is demonstrated in various laboratory
animal models.
ACCESSION NUMBER: 2002:428639 CAPLUS
DOCUMENT NUMBER: 136:395953
TITLE: Anti-proliferative drugs
INVENTOR(S): Gil-Ad, Irit; Weizman, Abraham
PATENT ASSIGNEE(S): Ramot University Authority for Applied Research & Industrial Development Ltd., Israel
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002043652	A2	20020606	WO 2001-IL1105	20011129
WO 2002043652	A3	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2430296	AA	20020606	CA 2001-2430296	20011129
AU 2002018467	A5	20020611	AU 2002-18467	20011129
EP 1347752	A2	20031001	EP 2001-998305	20011129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004029860	A1	20040212	US 2003-432875	20030916
PRIORITY APPLN. INFO.:			IL 2000-139975 A	20001129
			WO 2001-IL1105 W	20011129

L9 ANSWER 48 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB Selective norepinephrine reuptake inhibitors, e.g.tomoxetine, are used to treat anxiety disorders, especially obsessive-compulsive disorder.
ACCESSION NUMBER: 2002:391520 CAPLUS
DOCUMENT NUMBER: 136:363874
TITLE: Selective norepinephrine reuptake inhibitors for the treatment of anxiety disorders
INVENTOR(S): Thomasson, Holly Read; Michelson, David
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040006	A2	20020523	WO 2001-US27801	20011106
WO 2002040006	A3	20031224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2426069	AA	20020523	CA 2001-2426069	20011106
AU 2002017757	A5	20020527	AU 2002-17757	20011106
EP 1395253	A2	20040310	EP 2001-996376	20011106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004529073	T2	20040924	JP 2002-542380	20011106
US 2004034106	A1	20040219	US 2003-416294	20030507
NO 2003002156	A	20030513	NO 2003-2156	20030513
HR 2003000384	A1	20030831	HR 2003-384	20030514
PRIORITY APPLN. INFO.:			US 2000-249010P P	20001115
			US 2001-265362P P	20010131
			WO 2001-US27801 W	20011106

OTHER SOURCE(S): MARPAT 136:363874

L9 ANSWER 49 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The
peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.
ACCESSION NUMBER: 2002:332011 CAPLUS
DOCUMENT NUMBER: 136:355482
TITLE: Compositions comprising a polypeptide and an active agent
INVENTOR(S): Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randall J.
PATENT ASSIGNEE(S): New River Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034237	A1	20020502	WO 2001-US26142	20010822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6716452	B1	20040406	US 2000-642820	20000822
CA 2420590	AA	20020502	CA 2001-2420590	20010822
AU 2001086599	A5	20020506	AU 2001-86599	20010822
EP 1311242	A1	20030521	EP 2001-966056	20010822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004523480	T2	20040805	JP 2002-537291	20010822
US 2004127397	A1	20040701	US 2003-727565	20031205
PRIORITY APPLN. INFO.:			US 2000-642820 A	20000822
			US 2000-247613P P	20001114
			US 2000-247614P P	20001114
			US 2000-247615P P	20001114
			US 2000-247616P P	20001114
			US 2000-247617P P	20001114
			US 2000-247622P P	20001114
			US 2000-247630P P	20001114
			US 2000-247631P P	20001114

L9 ANSWER 49 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 2000-247632P	P	20001114
US 2000-247633P	P	20001114
US 2000-247556P	P	20001114
US 2000-247558P	P	20001114
US 2000-247559P	P	20001114
US 2000-247560P	P	20001114
US 2000-247561P	P	20001114
US 2000-247594P	P	20001114
US 2000-247595P	P	20001114
US 2000-247606P	P	20001114
US 2000-247607P	P	20001114
US 2000-247608P	P	20001114
US 2000-247609P	P	20001114
US 2000-247610P	P	20001114
US 2000-247611P	P	20001114
US 2000-247612P	P	20001114
US 2000-247620P	P	20001114
US 2000-247621P	P	20001114
US 2000-247634P	P	20001114
US 2000-247635P	P	20001114
US 2000-247698P	P	20001114
US 2000-247699P	P	20001114
US 2000-247701P	P	20001114
US 2000-247702P	P	20001114
US 2000-247797P	P	20001114
US 2000-247798P	P	20001114
US 2000-247799P	P	20001114
US 2000-247800P	P	20001114
US 2000-247801P	P	20001114
US 2000-247802P	P	20001114

L9 ANSWER 49 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 2000-247803P	P	20001114
US 2000-247804P	P	20001114
WO 2001-US26142	W	20010822

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L9 ANSWER 50 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Good regioselectivity and chirality transfer for aryl-substituted allyl units is achieved in allylic alkylations with a wide range of nucleophiles by using the highly active ruthenium catalyst (CpRu(cod)Cl). This method provides a route to antidepressants such as (-)-fluoxetine from (S)-ephedrine.

ACCESSION NUMBER: 2002:243136 CAPLUS
DOCUMENT NUMBER: 137:140298
TITLE: A stereospecific ruthenium-catalyzed allylic alkylation
AUTHOR(S): Trost, Barry M.; Fraisse, Pierre L.; Ball, Zachary T.
CORPORATE SOURCE: Department of Chemistry, Stanford University, Stanford, CA, 94305-5080, USA
SOURCE: Angewandte Chemie, International Edition (2002), 41(6), 1059-1061
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:140298

L9 ANSWER 51 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Studies were performed to determine the human enzymes responsible for the biotransformation of atomoxetine to its major metabolite, 4-hydroxyatomoxetine, and to a minor metabolite, N-desmethylatomoxetine. Utilizing human liver microsomes containing a full complement of cytochrome P 450 (P 450) enzymes, average Km and CLint values of 2.3 μM and 103 μl/min/mg, resp., were obtained for 4-hydroxyatomoxetine formation. Microsomal samples deficient in CYP2D6 exhibited average apparent Km and CLint values of 149 μM and 0.2 μl/min/mg, resp. In a human liver bank characterized for P 450 content, formation of 4-hydroxyatomoxetine correlated only to CYP2D6 activity. Of nine expressed P450s examined, 4-hydroxyatomoxetine was formed at a rate 475-fold greater by CYP2D6 compared with the other P450s. These results demonstrate that CYP2D6 is the enzyme primarily responsible for the formation of 4-hydroxyatomoxetine. Multiple P450s were found to be capable of forming 4-hydroxyatomoxetine when CYP2D6 was not expressed. However, the efficiency at which these enzymes perform this biotransformation is reduced compared with CYP2D6. The formation of the minor metabolite N-desmethylatomoxetine exhibited average Km and CLint values of 83 μM and 0.8 μl/min/mg, resp. Utilizing studies similar to those outlined above, CYP2C19 was identified as the primary enzyme responsible for the biotransformation of atomoxetine to N-desmethylatomoxetine. In summary, CYP2D6 was found to be the primary P 450 responsible for the formation of the major oxidative metabolite of atomoxetine, 4-hydroxyatomoxetine. Furthermore, these studies indicate that in patients with compromised CYP2D6 activity, multiple low-affinity enzymes will participate in the formation of 4-hydroxyatomoxetine. Therefore, coadministration of P 450 inhibitors to poor metabolizers of CYP2D6 substrates would not be predicted to decrease the clearance of atomoxetine in these individuals.

ACCESSION NUMBER: 2002:139958 CAPLUS
DOCUMENT NUMBER: 137:15251
TITLE: Identification of the human cytochromes P450 responsible for atomoxetine metabolism
AUTHOR(S): Ring, Barbara J.; Gillespie, Jennifer S.; Eckstein, James A.; Wrighton, Steven A.
CORPORATE SOURCE: Department of Drug Disposition, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA
SOURCE: Drug Metabolism and Disposition (2002), 30(3), 319-323
CODEN: DMDSAI; ISSN: 0090-9556
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L9 ANSWER 52 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Pharmaceutical compns. are disclosed for the treatment of attention deficit hyperactivity disorder (ADHD). The pharmaceutical compns. are comprised of a therapeutically effective combination of a nicotine receptor partial agonist and an anti-ADHD agent and a pharmaceutically acceptable carrier. The method of using these compds. is also disclosed.

ACCESSION NUMBER: 2002:104621 CAPLUS
DOCUMENT NUMBER: 136:145265
TITLE: A pharmaceutical composition for the treatment of attention deficit hyperactivity disorder (ADHD) comprising a nicotine receptor partial agonist and anti-ADHD agent
INVENTOR(S): Watsky, Eric Jacob; Coe, Jotham Wadsworth; Harrigan, Edmund Patrick; O'Neill, Brian Thomas; Sands, Steven Bradley
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 1177798	A2	20020206	EP 2001-306455		20010727
EP 1177798	A3	20030305			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
US 2002016334	A1	20020207	US 2001-865793		20010525
CA 2354237	AA	20020131	CA 2001-2354237		20010727
BR 2001003169	A	20020528	BR 2001-3169		20010731
JP 2002316949	A2	20021031	JP 2001-231554		20010731
US 2004220184	A1	20041104	US 2004-851826		20040521
PRIORITY APPLN. INFO.:			US 2000-221718P	P	20000731
			US 2001-865793	A1	20010525

L9 ANSWER 53 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The present invention pertains to methods for reducing the platelet activation state in an individual comprising administering a selective serotonin reuptake inhibitor (SSRI). The platelet activation state is reduced upon administering a SSRI, as measured by one or more platelet activation markers. The invention also relates to methods for treating or preventing an individual at risk for a vascular event, disease or disorder by administering a SSRI.

ACCESSION NUMBER: 2002:90620 CAPLUS
DOCUMENT NUMBER: 136:112659
TITLE: Methods of inhibiting platelet activation with selective serotonin reuptake inhibitors and treatment of cardiovascular disease
INVENTOR(S): Serebruany, Victor L.; Gurbel, Paul A.; O'Connor, Christopher M.
PATENT ASSIGNEE(S): Heartdrug Research, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. 6,245,782.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002013343	A1	20020131	US 2001-804689		20010312
US 6552014	B2	20030422			
US 6245782	B1	20010612	US 1999-312987		19990517
ZA 2001009994	A	20020826	ZA 2001-9994		20011205
PRIORITY APPLN. INFO.:			US 1999-312987	A2	19990517

L9 ANSWER 54 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Norepinephrine reuptake inhibitors, e.g., tomoxetine or its salts, reboxetine, duloxetine, are used to treat psoriasis. Thus, hard gelatin capsules contained tomoxetine-HCl 30.0, starch 305.0, and Mg stearate 5.0 mg/capsule.

ACCESSION NUMBER: 2001:676591 CAPLUS
DOCUMENT NUMBER: 135:216029
TITLE: Treatment of psoriasis with norepinephrine reuptake inhibitors
INVENTOR(S): Thomasson, Holly Read
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001066101	A2	20010913	WO 2001-US5260		20010220
WO 2001066101	A3	20020207			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2400571	AA	20010913	CA 2001-2400571		20010220
EP 1267859	A2	20030102	EP 2001-918185		20010220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
BR 2001008980	A	20030603	BR 2001-8980		20010220
JP 2003525899	T2	20030902	JP 2001-564754		20010220
ZA 2002005266	A	20031001	ZA 2002-5266		20020701
US 2003045585	A1	20030306	US 2002-203403		20020807
US 6683114	B2	20040127			
NO 2002004236	A	20020905	NO 2002-4236		20020905
PRIORITY APPLN. INFO.:			US 2000-187508P	P	20000307
			WO 2001-US5260	W	20010220

OTHER SOURCE(S): MARPAT 135:216029

L9 ANSWER 55 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The present invention provides a method of treating and preventing obesity and related co-morbid conditions comprising the administration of a therapeutically effective amount of one or more monoamine reuptake inhibitors which are serotonin reuptake inhibitors and/or noradrenaline reuptake inhibitors and a 5-HT1A agonist to a patient in need thereof. Monoamine reuptake inhibitors such as sibutramine are useful in treating obesity but have cardiovascular side-effects which can be diminished by administration of a 5-HT1A agonist such as flesinoxan. An example is given in which flesinoxan reduces the cardiovascular (blood pressure, heart rate) effects of sibutramine in rats.

ACCESSION NUMBER: 2001:635946 CAPLUS
DOCUMENT NUMBER: 135:190433
TITLE: Therapeutic agents for treating obesity
INVENTOR(S): Heal, David John; Cheetham, Sharon Crawford
PATENT ASSIGNEE(S): Knoll Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001062341	A2	20010830	WO 2001-EP1894		20010220
WO 2001062341	A3	20020131			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2400797	AA	20010830	CA 2001-2400797		20010220
AU 2001052135	A5	20010903	AU 2001-52135		20010220
EP 1259292	A2	20021127	EP 2001-925343		20010220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003523410	T2	20030805	JP 2001-561399		20010220
US 2003130355	A1	20030710	US 2002-204392		20021112
PRIORITY APPLN. INFO.:			GB 2000-4003	A	20000222
			WO 2001-EP1894	W	20010220

L9 ANSWER 56 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A composition comprising: (a) a pharmaceutically effective amount of one or more norepinephrine reuptake inhibitors or a pharmaceutically effective salt thereof; and (b) a pharmaceutically effective amount of one or more antimuscarinic agents or a pharmaceutically effective salt thereof is provided. The composition is useful in treating disorders or diseases of the central nervous system, and particularly useful in treating incontinence. A composition was prepared containing reboxetine in either its racemic of (S,S) enantiomer forms with tolterodine.

ACCESSION NUMBER: 2001:635879 CAPLUS
DOCUMENT NUMBER: 135:200472
TITLE: Norepinephrine reuptake inhibitor and antimuscarinic agent combinations
INVENTOR(S): Rogosky, Karen; Jorn, Deborah
PATENT ASSIGNEE(S): Pharmacia & Upjohn Co., USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062236	A2	20010830	WO 2001-US3698	20010123
WO 2001062236	A3	20020307		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1257277	A2	20021120	EP 2001-910421	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003523382	T2	20030805	JP 2001-561303	20010123
NZ 520975	A	20040326	NZ 2001-520975	20010123
CA 2399442	AA	20010830	CA 2001-2399442	20010223
AU 2001038028	A5	20010903	AU 2001-38028	20010223
US 2002010216	A1	20020124	US 2001-792718	20010223

PRIORITY APPLN. INFO.: US 2000-184790P P 20000224
WO 2001-US3698 W 20010123

L9 ANSWER 57 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Preferential delivery via electrotransport of a preferred isomeric form of a pharmaceutically active chiral compound from a mixture of the isomeric forms of said compound is provided. A method of decreasing the delivery via electrotransport of a less preferred isomer of a drug is also provided. Following electrotransport administration of ketorolac, the mean amount of R isomer absorbed was lower than that of the S isomer.

ACCESSION NUMBER: 2000:754414 CAPLUS
DOCUMENT NUMBER: 133:325631
TITLE: Stereospecific delivery of a drug using electrotransport
INVENTOR(S): Gupta, Suneel K.; Sathyan, Gayatri; Padmanabhan, Rama
PATENT ASSIGNEE(S): ALZA Corporation, USA
SOURCE: U.S., 22 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6136327	A	20001024	US 1997-982245	19971201
JP 2001524364	T2	20011204	JP 2000-522969	19981130

PRIORITY APPLN. INFO.: US 1997-982245 A 19971201
WO 1998-US25387 W 19981130

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 58 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB ArCH(OAr1)CH2CH2NMeG [Ar = Ph, 2-thienyl; Ar1 = 1-naphthyl, 2-methoxyphenyl, 2-(methylthio)phenyl, 2-methylphenyl; G = H, Me] are prepared by reaction of the alkoxides of ArCH(OH)CH2CH2NMeG with Ar1X (X = F, Cl) in 1,3-dimethyl-2-imidazolidinone or N-methyl-2-pyrrolidinone as solvent. Thus, 10 g 3-hydroxy-N-methyl-3-phenylpropylamine and 7.5 g K tert-butoxide are heated with 20 mL 2-fluorotoluene in 25 mL 1,3-dimethyl-2-imidazolidinone at 110° for 20 h to give N-methyl-3-(2-methylphenoxy)-3-phenylpropylamine, which was combined with (S)-(+)-mandelic acid in order to isolate the R isomer (as the hydrochloride) after decomposition of the salt.

ACCESSION NUMBER: 2000:742056 CAPLUS
DOCUMENT NUMBER: 133:296273
TITLE: Methods for preparing 3-aryloxy-3-arylpropylamines and their intermediates
INVENTOR(S): Kjell, Douglas Patton; Lorenz, Kurt Thomas
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

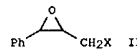
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061540	A1	20001019	WO 2000-US6423	20000322
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2362185	AA	20001019	CA 2000-2362185	20000322
EP 1171417	A1	20020116	EP 2000-917868	20000322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002541235	T2	20021203	JP 2000-610817	20000322
US 6541668	B1	20030401	US 2001-936468	20010912

PRIORITY APPLN. INFO.: US 1999-128480P P 19990409
WO 2000-US6423 W 20000322

OTHER SOURCE(S): MARPAT 133:296273
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 59 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

GI



II

AB (S)-oxetine enantiomers such as tomoxetine, fluoxetine, and nisoxetine, which are serotonergic appetite depressants, represented by formula PhCH(OY)CH2CH2NR1R2 (I; R1 = H, C1-5 alkyl; R2 = C1-5 alkyl; Y = 4-trifluoromethylphenyl, 2-methylphenyl, 2-ethoxyphenyl; X = halo, HO, ester, amino) are prepared by method 1 involving steps (a) conversion of propiophenone represented by formula PhCOCH2CH2X (X = same as above) into racemic alcs. represented by formula PhCHOHCH2CH2X, under nonchiral conditions and (b) optical resolution of the latter racemic alcs. to (R)- and (S)-enantiomer with at least 95% enantiomeric purity by pseudo-moving bed chromatog. separation using chiral adsorbent and conversion of the (S)-alc. enantiomer into (S)-I or method 2 involving steps (a) selective conversion of 3-substituted 1-phenyl-1-propene represented by formula PhCH:CHCH2X (X = same as above) into racemic epoxides (II: X = same as above) under nonchiral conditions and conversion of the racemic epoxides into racemic I or (b) optical resolution of the latter racemic epoxides to (R)- and (S)-enantiomer with at least 95% enantiomeric purity by pseudo-moving bed chromatog. separation using chiral adsorbent and conversion of the (S)-epoxide enantiomer into (S)-I. Undesired (R)-alc. and (R)-epoxide enantiomers are racemized and recycled to the optical resolution steps in methods 1 and 2. In this process, racemic precursors undergo optical resolution with high optical purity at the early stage of the oxetine synthesis and the optical purity of the precursors is maintained and carried over to the products.

ACCESSION NUMBER: 2000:731520 CAPLUS
DOCUMENT NUMBER: 133:296272
TITLE: Method for preparation of (S)-oxetine enantiomers
INVENTOR(S): Gattuso, Marion J.
PATENT ASSIGNEE(S): UOP Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000290239	A2	20001017	JP 1999-87304	19990329

PRIORITY APPLN. INFO.: JP 1999-87304 19990329

OTHER SOURCE(S): MARPAT 133:296272

L9 ANSWER 59 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L9 ANSWER 60 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The discriminative stimulus (DS) effects of 4-aminopyridine (4-AP) were evaluated in 36 male Sprague-Dawley rats that were trained to discriminate 4-AP from saline in a standard two-lever food reinforced drug discrimination procedure. 4-AP along with its structural analogs 3-aminopyridine (3-AP), 2-aminopyridine (2-AP), and 2,3-diaminopyridine (2,3-DIAP) produced dose-dependent increases in the percentage of responses on the 4-AP-associated lever with full substitution at one or more doses. 2,6-Diaminopyridine (2,6-DIAP) and 3,4-diaminopyridine (3,4-DIAP) produced dose-dependent increases in the percentage of responses on the 4-AP-associated lever but only partially substituted for 4-AP. Neither 4-dimethylaminopyridine (4-DMAP) nor pyridine substituted for 4-AP. Substitution studies were also conducted with indirect dopamine, norepinephrine, serotonin, and acetylcholine agonists, and γ-aminobutyric acid A (GABAA) agonists and antagonists. The norepinephrine re-uptake inhibitor tomoxetine, but not nisoxetine or imipramine, produced dose-dependent increases in the percentage of responses on the 4-AP-associated lever and partially substituted for 4-AP. In addition, antagonism studies were conducted using indirect dopamine, norepinephrine, serotonin, acetylcholine antagonists, and GABAA agonists as pretreatments to the training dose of 4-AP. The benzodiazepine agonists chlordiazepoxide and diazepam dose dependently attenuated the DS effects of 4-AP. The present results demonstrate that the K-channel blocker 4-AP can be trained as a DS in rats and the DS effects of 4-AP are likely mediated through blockade of voltage-dependent K-channels. The results also demonstrate a novel interaction between benzodiazepines and K-channels.

ACCESSION NUMBER: 2000:728414 CAPLUS
DOCUMENT NUMBER: 134:13285
TITLE: Pharmacological characterization of the discriminative stimulus effects of the potassium channel blocker 4-aminopyridine in rats
AUTHOR(S): Brandsgaard, Roxanne; Barrett, James E.; Rosenzweig-Lipson, Sharon
CORPORATE SOURCE: Wyeth-Ayerst Research, Princeton, NJ, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 295(1), 382-391
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 61 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB This invention relates to the use of a CYP2D6 inhibitor in combination with a drug having CYP2D6-catalyzed metabolism, wherein the drug and the CYP2D6 inhibitor are not the same compound; and pharmaceutical compns. for said use.

ACCESSION NUMBER: 2000:725447 CAPLUS
DOCUMENT NUMBER: 133:301178
TITLE: Use of CYP2D6 inhibitors in combination therapies
INVENTOR(S): Obach, Ronald Scott
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059486	A2	20001012	WO 2000-IB304	20000320
WO 2000059486	C1	20020725		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2367052	AA	20001012	CA 2000-2367052	20000320
BR 2000009564	A	20020108	BR 2000-9564	20000320
EP 1242058	A1	20020925	EP 2000-909570	20000320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EE 200100524	A	20021216	EE 2001-524	20000320
JP 2003523936	T2	20030812	JP 2000-609050	20000320
AU 774923	B2	20040715	AU 2000-31850	20000320
NZ 514466	A	20041029	NZ 2000-514466	20000320
US 2003144220	A1	20030731	US 2000-528978	20000321
HR 2001000722	A1	20020831	HR 2001-722	20011004
ZA 2001008158	A	20030724	ZA 2001-8158	20011004
NO 2001004858	A	20011205	NO 2001-4858	20011005
BG 106075	A	20020628	BG 2001-106075	20011101
US 2004018253	A1	20040129	US 2003-622301	20030718
US 2004028755	A1	20040212	US 2003-624123	20030721

PRIORITY APPLN. INFO.: US 1999-128136P P 19990407
WO 2000-IB304 W 20000320
US 2000-528978 A3 20000321

L9 ANSWER 62 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The title processes comprises stereoselective etherification of an alkoxide (sic) of (R)-PhCH(OR)CH2CH2NMe2 (I; R = H) by 2-XC6H4Z1 [X = halo, Z1 = e.g., CH(OR1)OR11 or CH:NR2; R1,R11 = alkyl or CH2Ph; R1R11 = alkylene; R2 = alkyl or (un)substituted Ph] to give I (R = C6H4Z1-2) followed by conversion of Z1 to Me.

ACCESSION NUMBER: 2000:707122 CAPLUS
DOCUMENT NUMBER: 133:281603
TITLE: Preparation of tomoxetine
INVENTOR(S): Heath, Perry Clark; Ratz, Andrew Michael; Weigel, Leland Otto
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058262	A1	20001005	WO 2000-US2527	20000229
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-126701P P 19990329

OTHER SOURCE(S): CASREACT 133:281603; MARPAT 133:281603
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 63 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The locus coeruleus (LC) is the largest norepinephrinergic cell group in the central nervous system and contains a high d. of norepinephrine (NE) uptake sites. Alc.-preferring (AP) rats and high-alc.-drinking (HAD) rats are selectively bred for high alc. preference, whereas alc.-nonpreferring (NP) rats and low-alc.-drinking (LAD) rats are bred for low alc. preference. However, it is unknown whether NE uptake sites in the LC are associated with alc. preference in AP and HAD rats when compared with their resp. control rats, NP and LAD rats. This study was designed to examine this question. Animals were decapitated and brains were removed, frozen with dry ice powder, and stored in a deep freezer. The LC tissue blocks were cut into 14 μ cryostat sections, collected on glass slides, and incubated with 0.6 nM [3H]-tomoxetine in 50 mM Tris-HCl buffer system. For nonspecific binding, 1 μM desipramine was added to the radioactive ligand. Sections were rinsed, quickly dried, and processed for quant. autoradiog. In addition, galanin content in the LC was also studied. The LC possessed a high d. of [3H]-tomoxetine binding sites. There were fewer tomoxetine binding sites (fmol/mg protein) in the AP rats (433.0 ± 8.1) than in the NP rats (495.6 ± 3.7). HAD rats (386.5 ± 13.2) also possessed fewer tomoxetine binding sites than LAD rats (458.7 ± 10.1). Galanin content in the LC was similar between AP and NP rats and between HAD and LAD rats. Because both AP rats and HAD rats were selectively bred for alc. preference, the finding of consistently low levels of [3H]-tomoxetine binding in the LC of these two lines of rats with high alc. preference suggests that down-regulation of NE transporters in the LC of AP and HAD rats may be associated with alc.-seeking behavior. A possible involvement of the coerulear NE uptake sites in depression is also discussed. Galanin in the LC may not relate to alc. preference.

ACCESSION NUMBER: 2000:415187 CAPLUS
DOCUMENT NUMBER: 133:173275
TITLE: Norepinephrine uptake sites in the locus coeruleus of rat lines selectively bred for high and low alcohol preference: a quantitative autoradiographic binding study using [3H]-tomoxetine
AUTHOR(S): Hwang, Bang H.; Wang, Guo-Ming; Wong, David T.; Lumeng, Lawrence; Li, T.-K.
CORPORATE SOURCE: Department of Anatomy, School of Medicine, Indiana University, Indianapolis, IN, USA
SOURCE: Alcoholism: Clinical and Experimental Research (2000), 24(5), 588-594
CODEN: ACRSDM; ISSN: 0145-6008
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 64 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB 3-Chloro-1-phenylpropan-1-ol and the corresponding butanoate, 3-chloro-1-phenylpropyl butanoate, were kinetically resolved using lipase B from Candida antarctica catalysis by transesterification and hydrolysis resp. The resulting chiral building blocks, (S)- and (R)-3-chloro-1-phenylpropanol, were converted into both enantiomers of the antidepressant drugs Fluoxetine, Tomoxetine and Nisoxetine.

ACCESSION NUMBER: 2000:361406 CAPLUS
DOCUMENT NUMBER: 133:237610
TITLE: Chemoenzymatic synthesis of the non-tricyclic antidepressants Fluoxetine, Tomoxetine and Nisoxetine
AUTHOR(S): Liu, Hui-Ling; Hoff, Bard Helge; Anthonsen, Thorleif
CORPORATE SOURCE: Department of Chemistry, Norwegian University of Science and Technology, Trondheim, N-7491, Norway
SOURCE: Perkin 1 (2000), (11), 1767-1769
CODEN: PERKF9
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:237610
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 65 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Pharmaceutical compns. which comprise R(-) fluoxetine and one or more other biol. active compds. e.g. a benzodiazepine compound, a tricyclic antidepressant, a 5-HT1A receptor antagonist, a 5-HT3 receptor agonist, a β-adrenergic antagonist, an antipsychotic agent, an anti-anxiolytic or other psychotropic drug, are disclosed. Methods of treating or preventing a disease or disorder, especially a psychotic or psychiatric disease or disorder, using the above pharmaceutical composition or by administering a R(-)fluoxetine in combination with one or more other biol. active compds. are also disclosed. Methods of treating patients having or at risk of having AIDS or HIV infection, cancer, cardiac disorder, post-myocardial depression and post-traumatic stress disorder using optically pure R(-)fluoxetine in combination with one or more other biol. active compds. are further disclosed.

ACCESSION NUMBER: 1999:763863 CAPLUS
DOCUMENT NUMBER: 132:6368
TITLE: Compositions and methods employing R(-)fluoxetine and other active ingredients
INVENTOR(S): Barberich, Timothy J.; Rubin, Paul D.; Handley, Dean A.
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9961014	A2	19991202	WO 1999-US11725		19990527
WO 9961014	A3	20000720			
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9941006	A1	19991213	AU 1999-41006		19990527
US 2002151543	A1	20021017	US 2002-158886		20020603
PRIORITY APPLN. INFO.:			US 1998-86262	A	19980528
			US 1998-177703	B2	19981023
			WO 1999-US11725	W	19990527
			US 2000-664732	B3	20000919

L9 ANSWER 66 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A review with 52 refs. Lilly is developing tomoxetine, a norepinephrine uptake inhibitor, for the potential treatment of attention deficit hyperactivity disorder (ADHD) and depression. The drug is undergoing phase II clin. testing in 7 to 13-yr old patients with attention deficit disorders [275533], [326984]. In a randomized placebo-controlled phase II study in adults with childhood-onset and persistent ADHD, tomoxetine (40 mg/day increasing to 80 mg/day for 3 wk) reduced symptoms measured on the ADHD rating scale [326909]. Tomoxetine was first investigated by Lilly in the 1980s as a potential treatment for depressive illness. The compound was selected from a series of potent inhibitors of norepinephrine reuptake, and reached phase II clin. trials for depression in 1990. Development appeared to stop at that time, in spite of some evidence that tomoxetine was fairly effective [273943]. In 1996, Lilly apparently restarted preclin. development of tomoxetine as a potential therapy for ADHD, and submitted EP-00721777 claiming tomoxetine's utility for this disorder in July of that year [273956]. In Feb. 1999, Deutsche Bank predicted sales of $100 million in 2001 rising to $400 million in 2003 [316821].

ACCESSION NUMBER: 1999:661307 CAPLUS
DOCUMENT NUMBER: 131:266451
TITLE: Tomoxetine (Eli Lilly)
AUTHOR(S): Preti, Antonio
CORPORATE SOURCE: Psychiatry Branch, Genneruxi Medical Center, Cagliari, 09129, Italy
SOURCE: Current Opinion in Central & Peripheral Nervous System Investigational Drugs (1999), 1(4), 514-520
CODEN: COCDFA; ISSN: 1464-844X
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 67 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A method for producing a potentiating effect on a therapeutic action of an agent which is selected from a serotonin re-uptake inhibitor, a norepinephrine re-uptake inhibitors, both a serotonin and norepinephrine re-uptake inhibitor, and an atypical antidepressant in a warm blooded mammal, comprises administering to said mammal an effective amount of moxonidine, or a pharmaceutically acceptable salt thereof. A tablet contained moxonidine 0.300, lactose 95.700, povidone 0.700, crospovidone 3.000, magnesium stearate 0.300, hydroxypropyl Me cellulose 1.300, Et cellulose 1.200, PEG 0.250, talc 0.975, red ferric oxide 0.025, and titanium dioxide 1.250 mg. Moxonidine at 0.2 mg twice daily when combined with 20 mg fluoxetine daily had synergistic effects in patients suffering major depression.

ACCESSION NUMBER: 1999:282100 CAPLUS
DOCUMENT NUMBER: 130:316651
TITLE: Synergistic pharmaceutical compositions containing moxonidine
INVENTOR(S): Perry, Kenneth Wayne
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920279	A1	19990429	WO 1998-US21418	19981009
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306233	AA	19990429	CA 1998-2306233	19981009
AU 9896928	A1	19990510	AU 1998-96928	19981009
EP 919234	A2	19990602	EP 1998-308225	19981009
EP 919234	A3	19990825		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
ZA 9809251	A	20000410	ZA 1998-9251	19981009
US 6066643	A	20000523	US 1998-169369	19981009
JP 2001520195	T2	20011030	JP 2000-516676	19981009

PRIORITY APPLN. INFO.: US 1997-62282P P 19971017
WO 1998-US21418 W 19981009

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 68 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A simple, systematic method was developed for rapidly screening potential capillary electrophoresis (CE) separation conditions for small, amine-containing enantiomers. During method development, 39 pairs of enantiomers were studied and partial or complete separation was achieved in every case. Baseline resolution was achieved by these initial screening conditions in over half of the cases. The screening strategy uses a bare fused silica capillary and a pH 2.5 amine-modified phosphate buffer containing one of the selected cyclodextrins (CD): dimethyl-β-CD, hydroxypropyl-β-CD, hydroxypropyl-α-CD, hydroxypropyl-γ-CD and sulfated-β-CD. An addnl. set of compds. were screened by this approach to demonstrate the validity of the method. The paper outlines the exptl. work carried out to develop the screen and describes how one might implement it for a new compound

ACCESSION NUMBER: 1999:244205 CAPLUS
DOCUMENT NUMBER: 130:346558
TITLE: Systematic screening approach for chiral separations of basic compounds by capillary electrophoresis with modified cyclodextrins
AUTHOR(S): Liu, Li; Nussbaum, Mark A.
CORPORATE SOURCE: Pharmaceutical Sciences Division, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, 46285, USA
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1999), 19(5), 679-694
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 69 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Norepinephrine reuptake inhibitors (e.g. duloxetine) are used to treat oppositional defiant disorder.

ACCESSION NUMBER: 1999:231508 CAPLUS
DOCUMENT NUMBER: 130:262137
TITLE: Norepinephrine reuptake inhibitor for treatment of oppositional defiant disorder
INVENTOR(S): Heiligenstein, John Harrison
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9915176	A1	19990401	WO 1998-US18114	19980901
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2304115	AA	19990401	CA 1998-2304115	19980901
AU 9891282	A1	19990412	AU 1998-91282	19980901
AU 740109	B2	20011101		
BR 9812357	A	20000912	BR 1998-12357	19980901
TR 200000755	T2	20000921	TR 2000-200000755	19980901
JP 2001517627	T2	20011009	JP 2000-512545	19980901
NZ 502810	A	20020301	NZ 1998-502810	19980901
US 6028070	A	20000222	US 1998-156289	19980917
EP 919236	A1	19990602	EP 1998-307650	19980921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2000001458	A	20000321	NO 2000-1458	20000321

PRIORITY APPLN. INFO.: US 1997-59629P P 19970923
WO 1998-US18114 W 19980901

OTHER SOURCE(S): MARPAT 130:262137
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 70 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Norepinephrine reuptake inhibitors (e.g. duloxetine) are used to treat conduct disorder.

ACCESSION NUMBER: 1999:231496 CAPLUS
DOCUMENT NUMBER: 130:262136
TITLE: Norepinephrine reuptake inhibitors for treatment of conduct disorder
INVENTOR(S): Heiligenstein, John Harrison
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9915163	A1	19990401	WO 1998-US18103	19980901
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2304657	AA	19990401	CA 1998-2304657	19980901
AU 9890417	A1	19990412	AU 1998-90417	19980901
AU 740192	B2	20011101		
BR 9812371	A	20000919	BR 1998-12371	19980901
TR 200000756	T2	20000921	TR 2000-200000756	19980901
JP 2001517619	T2	20011009	JP 2000-512532	19980901
NZ 502853	A	20020828	NZ 1998-502853	19980901
US 6184222	B1	20010206	US 1998-156285	19980917
EP 919235	A1	19990602	EP 1998-307630	19980921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2000001479	A	20000322	NO 2000-1479	20000322

PRIORITY APPLN. INFO.: US 1997-59628P P 19970923
WO 1998-US18103 W 19980901

OTHER SOURCE(S): MARPAT 130:262136
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 71 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB In an effort to identify novel binding sites for cocaine and its analogs, the authors carried out binding studies with the high-affinity and selective ligand [125I]RTI-121 in rat frontal cortical tissue. Very low densities of binding sites were found. Saturation anal. revealed that the binding was to both high- and low-affinity sites. Pharmacol. competition studies were carried out with inhibitors of the dopamine, norepinephrine, and serotonin transporters. The various transporter inhibitors inhibited the binding of 15 pM [125I]RTI-121 in a biphasic fashion following a two-site binding model. The resultant data were complex and did not suggest a simple association with any single transporter. Correlational anal. supported the following hypothesis: [125I] RTI-121 binds to known transporters and not to novel sites; these include dopamine, norepinephrine, and serotonin transporters. Immunopptn. of transporters photoaffinity labeled with [125]RTI-82 and subsequent anal. of SDS-page gels revealed the presence of authentic dopamine transporters in these samples; displacement of the photoaffinity label occurred with a typical dopamine transporter pharmacol. These data are compatible with the binding properties of RTI-121 and the presence of several known transporters in the tissue studied.

ACCESSION NUMBER: 1998:506893 CAPLUS
DOCUMENT NUMBER: 129:225624
TITLE: Multiple binding sites for [125I]RTI-121 and other cocaine analogs in rat frontal cerebral cortex
AUTHOR(S): Boja, J. W.; Carroll, F. I.; Vaughan, R. A.; Kopajtic, T.; Kuhar, M. J.
CORPORATE SOURCE: Dept. of Pharmacology, N.E. Ohio Universities College of Medicine, Rootstown, OH, 44266, USA
SOURCE: Synapse (New York) (1998), 30(1), 9-17
CODEN: SYNAET; ISSN: 0887-4476
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 72 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Cocaine, which non-selectively blocks the reuptake of the monoamines serotonin, dopamine and norepinephrine, produces weak antinociceptive effects and increases the antinociceptive effects of low- to intermediate-efficacy mu opioid agonists in rhesus monkeys. In the present study, the antinociceptive effects of more selective monoamine reuptake inhibitors administered alone and in combination with mu opioid agonists were evaluated in rhesus monkeys using a warm-water tail-withdrawal assay of thermal nociception. Like cocaine, the selective serotonin reuptake inhibitors clomipramine (0.01-3.2 mg/kg) and fluoxetine (0.1-10 mg/kg) produced weak antinociceptive effects. Pretreatment with the serotonin receptor antagonist mianserin (0.032-0.32 mg/kg) produced rightward and downward shifts in the clomipramine dose-effect curve, suggesting that the effects of clomipramine were mediated by serotonin receptors. Combination of clomipramine with the low efficacy mu agonist nalbuphine or the intermediate efficacy mu agonist morphine produced more antinociception than did the mu agonists alone. Fluoxetine also produced a small leftward shift in the morphine dose-effect curve. The selective norepinephrine reuptake inhibitors nisoxetine (0.1-10 mg/kg) and tomoxetine (0.1-10 mg/kg) and the selective dopamine reuptake inhibitors bupropion (0.032-3.2 mg/kg) and GBR 12909 (0.1-10 mg/kg) did not produce antinociception or increase antinociception induced by nalbuphine or morphine. In fact, GBR 12909 produced dose-dependent allodynia and reduced the maximal antinociceptive effects of morphine. These results suggest that inhibition of serotonin reuptake is sufficient to produce weak antinociceptive effects and enhance the antinociceptive effects of low efficacy mu opioid agonists. These results also suggest that the effects of cocaine on serotonin reuptake may contribute to cocaine's antinociceptive effects in rhesus monkeys.

ACCESSION NUMBER: 1998:94039 CAPLUS
DOCUMENT NUMBER: 128:226105
TITLE: Antinociceptive effects of monoamine reuptake inhibitors administered alone or in combination with mu opioid agonists in rhesus monkeys
AUTHOR(S): Gatch, Michael B.; Negus, S. Stevens; Mello, Nancy K.
CORPORATE SOURCE: Alcohol and Drug Abuse Research Center, McLean Hospital-Harvard Medical School, Belmont, MA, 02178, USA
SOURCE: Psychopharmacology (Berlin) (1998), 135(1), 99-106
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 73 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Using radioligand binding assays, we determined the equilibrium dissociation consts. (KD's) for 37 antidepressants, three of their metabolites (desmethylcitalopram, desmethylsertraline, and norfluoxetine), some mood stabilizers, and assorted other compds. (some antiepileptics, Ca2+ channel antagonists, benzodiazepines, psychostimulants, antihistamines, and monoamines) for the human serotonin, norepinephrine, and dopamine transporters. Among the compds. that we tested, mazindol was the most potent at the human norepinephrine and dopamine transporters with KD's of 0.45±0.03 nM and 8.1±0.4 nM, resp. Sertraline (KD=25±2 nM) and nomifensine (56±3 nM) were the two most potent antidepressants at the human dopamine transporter. We showed significant correlations for antidepressant affinities at binding to serotonin (R=0.93), norepinephrine (R=0.97), and dopamine (R=0.87) transporters in comparison to their resp. values for inhibiting uptake of monoamines into rat brain synaptosomes. These data are useful in predicting some possible adverse effects and drug-drug interactions of antidepressants and related compds.

ACCESSION NUMBER: 1997:808034 CAPLUS
DOCUMENT NUMBER: 128:149531
TITLE: Pharmacological profile of antidepressants and related compounds at human monoamine transporters
AUTHOR(S): Tatsumi, Masahiko; Groshan, Karen; Blakely, Randy D.; Richelson, Elliott
CORPORATE SOURCE: San Pablo Road, Mayo Clinic Jacksonville, Jacksonville, FL 32224, 4500, USA
SOURCE: European Journal of Pharmacology (1997), 340(2/3), 249-258
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 74 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB It has been demonstrated that castration alters the functioning of the olfactory bulb (OB)-norepinephrine (NE) system. In the present experiment, we examined one of the mechanisms by which castration modulates the OB-NE system by comparing NE uptake activity between intact and castrated male rats as studied using an in vitro superfusion technique. To accomplish this goal, NE output from the OB of intact and castrated male rats in response to infusion with two different drugs which alter NE uptake functions, tomoxetine and talsupram, were tested. Overall, NE outputs in response to tomoxetine were significantly higher in the castrated than in intact rats and both groups were significantly greater than non-infused controls. For the talsupram infusion group, NE outputs from the castrated, but not intact rats, were significantly greater than controls. No statistically significant differences were detected between the castrated and intact rats. These results demonstrate that castration alters the NE uptake activities in response to these noradrenergic uptake blockers and suggest that one mechanism by which castration alters OB-NE functioning is through reducing the uptake activity of NE within the OB. Such findings have important implications for olfactory-based learning and memory/recognition processes which are believed to involve the OB-NE system and are altered following castration.

ACCESSION NUMBER: 1997:795642 CAPLUS
DOCUMENT NUMBER: 128:97995
TITLE: Castration reduces olfactory bulb norepinephrine transporter function as indicated by responses to noradrenergic uptake blockers
AUTHOR(S): Shang, Yili; Dluzen, Dean E.
CORPORATE SOURCE: State Route 44, P.O. Box 95, Department of Anatomy, Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272-0095, 4209, USA
SOURCE: Brain Research (1998), 779(1,2), 119-124
CODEN: BRREAP; ISSN: 0006-8993
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 75 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB Exhaustive conformational analyses on four selective serotonin reuptake inhibitors resulted in a pharmacophoric model explaining observed differences in enantioselectivities. A number of test compds. from a diverse set of chemical structures was included in the evaluation of the model. Furthermore, selectivity towards noradrenaline reuptake is explained.

ACCESSION NUMBER: 1997:545611 CAPLUS
DOCUMENT NUMBER: 127:199618
TITLE: A stereoselective pharmacophoric model of the serotonin re-uptake site
AUTHOR(S): Gundertofte, Klaus; Bogeso, Klaus P.; Liljefors, Tommy
CORPORATE SOURCE: Research and Development, Copenhagen, DK-2500, Den.
SOURCE: Computer-Assisted Lead Finding and Optimization: Current Tools for Medicinal Chemistry, [European Symposium on Quantitative Structure-Activity Relationships], 11th, Lausanne, Sept. 1-6, 1996 (1997)
, Meeting Date 1996, 445-459. Editor(s): Van de Waterbeemd, Han; Testa, Bernard; Folkers, Gerd. Verlag Helvetica Chimica Acta: Basel, Switz.
CODEN: 64VEAH
DOCUMENT TYPE: Conference
LANGUAGE: English

L9 ANSWER 76 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB The dissociation rates of [3H]nisoxetine, [3H]GBR 12935 and [3H]citalopram from, resp., the rat brain noradrenaline, dopamine and 5-HT transporters were found to be markedly affected by several drugs. Sertraline strongly attenuated the rate of dissociation of [3H]nisoxetine from the noradrenaline transporter, while citalopram strongly attenuated that of [3H]citalopram from the 5-HT transporter. The effects of both drugs were stereospecific. Less potent affinity-modulating drugs were identified with regards to [3H]GBR 12935 dissociation from the dopamine transporter. All three neuronal monoamine transporters may thus have specific affinity-modulating sites which change the function of the transporters with possible implications for the reuptake of monoamines released during synaptic activity.

ACCESSION NUMBER: 1997:272250 CAPLUS
DOCUMENT NUMBER: 126:339164
TITLE: An affinity-modulating site on neuronal monoamine transport proteins
AUTHOR(S): Plenge, Per; Mellerup, Erling T.
CORPORATE SOURCE: Laboratory of Neuropsychiatry, Department of Pharmacology, University of Copenhagen, Copenhagen, DK-2100, Den.
SOURCE: Pharmacology & Toxicology (Copenhagen) (1997), 80(4), 197-201
CODEN: PHTOEH; ISSN: 0901-9928
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 77 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB Tomoxetine, a norepinephrine uptake inhibitor, is used to treat attention-deficit/hyperactivity disorder.

ACCESSION NUMBER: 1996:483626 CAPLUS
DOCUMENT NUMBER: 125:132798
TITLE: Use of tomoxetine for the treatment of attention deficit-hyperactivity disorder
INVENTOR(S): Heiligenstein, John Harrison; Tollefson, Gary Dennis
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 4 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 721777	A2	19960717	EP 1996-300157	19960109
EP 721777	A3	19970305		
EP 721777	B1	20020828		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
US 5658590	A	19970819	US 1995-371341	19950111
CA 2209735	AA	19960718	CA 1996-2209735	19960104
CA 2209735	C	20021001		
WO 9621430	A1	19960718	WO 1996-US91	19960104
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ				
RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9646938	A1	19960731	AU 1996-46938	19960104
AU 688665	B2	19980312		
BR 9606903	A	19971021	BR 1996-6903	19960104
CN 1168095	A	19971217	CN 1996-191412	19960104
JP 10512262	T2	19981124	JP 1996-521732	19960104
NZ 301500	A	20000728	NZ 1996-301500	19960104
RU 2163802	C2	20010310	RU 1997-113060	19960104
RO 118374	B1	20030530	RO 1997-1260	19960104
CZ 292226	B6	20030813	CZ 1997-2145	19960104
PL 187573	B1	20040831	PL 1996-321273	19960104
AT 222757	E	20020915	AT 1996-300157	19960109
PT 721777	T	20021129	PT 1996-300157	19960109
ES 2181845	T3	20030301	ES 1996-300157	19960109
NO 9703170	A	19970902	NO 1997-3170	19970708
FI 9702922	A	19970709	FI 1997-2922	19970709

PRIORITY APPLN. INFO.: US 1995-371341 A 19950111
WO 1996-US91 W 19960104

L9 ANSWER 78 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB (S)-1-Phenyl-3-buten-1-ol (1), prepared in high optical purity by enzymic resolution of the racemate, is a convenient building block for the synthesis of (R)-fluoxetine (7a) and (R)-tomoxetine (7b). Compound 1 was converted to the title drugs by etherification with appropriate phenols under Mitsunobu conditions, ozonolysis of the terminal double bond, mesylation of the resulting alc. and substitution with methylamine.

ACCESSION NUMBER: 1996:432302 CAPLUS
DOCUMENT NUMBER: 125:221272
TITLE: An efficient chemoenzymic route to the antidepressants (R)-fluoxetine and (R)-tomoxetine
AUTHOR(S): Bracher, Franz; Litz, Thomas
CORPORATE SOURCE: Institut fur Pharmazeutische Chemie, Technischen Universitat Braunschweig, Braunschweig, 38106, Germany
SOURCE: Bioorganic & Medicinal Chemistry (1996), 4(6), 877-880
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 79 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB This experiment was designed to elucidate the neurotransmitter systems that mediate the discriminative stimulus effects of methamphetamine. Pigeons were trained to peck 1 key following saline injections and a 2nd key following methamphetamine injections (1.0 or 1.7 mg/kg, i.m.). Substitution tests revealed drug-appropriate responding following administration of the psychomotor stimulants methamphetamine, amphetamine and cocaine, the dopamine (DA) reuptake inhibitor bupropion, the norepinephrine (NE) reuptake inhibitors imipramine and tomoxetine, and the serotonin (5-HT) releaser fenfluramine. Saline-key responding occurred following administration of the D1 agonist SKF-38393, the D1 antagonist SCH-23390, the α2-receptor agonist clonidine, the α1-antagonist prazosin, the nonselective β-antagonist propranolol and the selective 5-HT reuptake inhibitor fluoxetine. The D2/D3 agonist quinpirole produced drug-appropriate responding in 2 pigeons and partial substitution in the remaining 2 pigeons. The 5HT1A agonist 8-OH-DPAT produced drug-appropriate responding at higher doses (0.3-1.0 mg/kg), whereas much lower doses (0.003-0.1 mg/kg) antagonized the methamphetamine stimulus. The stimulus effects of methamphetamine were attenuated by pretreatment with prazosin, SCH-23390 and eticlopride, whereas pretreatment with propranolol and the 5-HT3 antagonist MDL 72222 failed to attenuate reliably drug-induced key responding. These results suggest that NE and DA reuptake inhibition and 5-HT release mediate the discriminative stimulus effects of methamphetamine, as do the 5-HT1A and DA D1 and D2 receptors.

ACCESSION NUMBER: 1995:809369 CAPLUS
DOCUMENT NUMBER: 123:218304
TITLE: The discriminative stimulus effects of methamphetamine in pigeons
AUTHOR(S): Sasaki, J. E.; Tatham, T. A.; Barrett, J. E.
CORPORATE SOURCE: Dep. Psychiatry, Univ. Health Sci., Bethesda, MD, 20814, USA
SOURCE: Psychopharmacology (Berlin) (1995), 120(3), 303-10
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 80 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB (R)-[3H]tomoxetine is a radioligand that binds to the norepinephrine (NE) uptake site with high affinity but also binds to a second, lower-affinity site. The goal of the present study was to identify the nature of this low-affinity site by comparing the binding properties of (R)-[3H]tomoxetine with those of (R/S)-[3H]nisoxetine, a highly selective ligand for the NE uptake site. In homogenate binding studies, both radioligands bound to the NE uptake site with high affinity, whereas (R)-[3H]tomoxetine also bound to a second, lower-affinity site. The autoradiog. distribution of binding sites for both radioligands is consistent with the known distribution of NE-containing neurons. However, low levels of (R)-[3H]-tomoxetine binding were seen in the caudate-putamen, globus pallidus, olfactory tubercle, and zona reticulata of the substantia nigra, where (R/S)-[3H]nisoxetine binding was almost absent. In homogenates of the caudate-putamen, the NE uptake inhibitors desipramine and (R)-nisoxetine and the serotonin (5-HT) uptake inhibitor citalopram produced biphasic displacement curves. Autoradiog. studies using 10 nM (R)-nisoxetine to mask the binding of (R)-[3H]tomoxetine to the NE uptake site produced autoradiograms that were similar to those produced by [3H]citalopram. Therefore, (R)-[3H]tomoxetine binds to the NE uptake site with high affinity and the 5-HT uptake site with somewhat lower affinity.

ACCESSION NUMBER: 1995:579657 CAPLUS
DOCUMENT NUMBER: 122:306469
TITLE: Comparison of (R)-[3H]tomoxetine and (R/S)-[3H]nisoxetine binding in rat brain
AUTHOR(S): Gehlert, Donald R.; Schober, Douglas A.; Gackenheimer, Susan L.
CORPORATE SOURCE: Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, USA
SOURCE: Journal of Neurochemistry (1995), 64(6), 2792-800
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott-Raven
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 81 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Thionisoxetine, a novel analog of the potent and selective norepinephrine (NE) uptake inhibitor nisoxetine, was evaluated. Thionisoxetine more potently inhibited the uptake of [3H]NE into rat hypothalamic synaptosomes and the binding of [3H]nisoxetine to the NE transporter than did (R)-nisoxetine. The (R) enantiomer of this compound was more potent than the (S) enantiomer, having a Ki of 0.20 nM in [3H]nisoxetine binding. The (R) enantiomer was approx. 70-fold more potent in inhibiting [3H]NE uptake than [3H]5HT uptake. In rats, (R)-thionisoxetine prevented hypothalamic NE depletion by 6-hydroxydopamine with an ED50 of 0.21 mg/kg. Depletion of NE in peripheral nerves was accomplished by the administration of metaraminol to rats. In this paradigm, (R)-thionisoxetine prevented the depletion of heart NE with an ED50 of 3.4 mg/kg and depletion of urethral NE with an ED50 of 1.2 mg/kg. Thus, (R)-thionisoxetine is a potent and selective inhibitor of NE uptake in both central and peripheral tissues.

ACCESSION NUMBER: 1995:521791 CAPLUS
DOCUMENT NUMBER: 122:282104
TITLE: (R)-Thionisoxetine, a potent and selective inhibitor of central and peripheral norepinephrine uptake
AUTHOR(S): Gehlert, Donald R.; Hemrick-Leucke, Susan K.; Schober, Douglas A.; Krushinski, Joseph; Howbert, J. Jeffry; Robertson, David W.; Wong, David T.; Fuller, Ray W.
CORPORATE SOURCE: Central Nervous System Res., Lilly Res. Lab., Div. Eli Lilly and Co., Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Life Sciences (1995), 56(22), 1915-20
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 82 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Halogenated analogs of the potent norepinephrine (NE) uptake inhibitor, tomoxetine, were synthesized and their affinities for the serotonin (5HT) and NE uptake sites evaluated. One of the most potent was the 2-iodo substituted analog (289306) that inhibited [3H]tomoxetine binding to rat cerebral cortex with a Ki of 0.3 7 nM. The compound also inhibited the uptake of [3H]NE into rat hypothalamic synaptosomes with a Ki of 3.5 nM. This analog was significantly less potent at the 5HT uptake site, as exhibited by a Ki of 25 nM in the inhibition of [3H]paroxetine binding and a Ki of 121 nM in [3H]5HT uptake. The resolved (R) enantiomer (303926) was 10 times more potent as a [3H]NE uptake inhibitor and 29 times more potent as an inhibitor of [3H]tomoxetine binding than the (S) enantiomer (303884). Administration of 289306 to rats prior to an i.c.v. injection of 6-hydroxydopamine prevented the depletion of hypothalamic NE and Epi with ED50 values of 0.28 and 0.47 mg/kg, resp. Thus, 289306 was a potent inhibitor of NE uptake in vitro and in vivo. In addition, these compds. provide structures for potential ligands for the study of NE uptake sites by autoradiog., PET or SPECT imaging.

ACCESSION NUMBER: 1995:356183 CAPLUS
DOCUMENT NUMBER: 122:178224
TITLE: Novel halogenated analogs of tomoxetine that are potent and selective inhibitors of norepinephrine uptake in brain
AUTHOR(S): Gehlert, Donald R.; Schober, Douglas A.; Hemrick-Luecke, Susan K.; Krushinski, Joseph; Howbert, Jeffry; Robertson, David W.; Fuller, Ray W.; Wong, David T.
CORPORATE SOURCE: Central Nervous System Res., Lilly Research Lab., Indianapolis, IN, 46285, USA
SOURCE: Neurochemistry International (1995), 26(1), 47-52
CODEN: NEUIDS; ISSN: 0197-0186
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

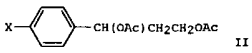
L9 ANSWER 83 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Binding to the dopamine transporter and inhibiting dopamine reuptake are considered important factors in regulating behavioral effects of cocaine. One prominent behavioral effect of cocaine and other dopamine uptake inhibitors is the stimulation of locomotor activity. To examine the relationship between action at the dopamine transporter and behavior, the displacement of [3H]WIN 35,428 (CFT naphthalene sulfate; 2-β-carbomethoxy-3-β-(4-fluorophenyl)tropane-1,5-naphthalene disulfonate) binding in rat caudate putamen by cocaine and other uptake inhibitors was compared with stimulation of mouse locomotor activity. There was a significant correlation among affinities for binding and potencies for stimulating activity for cocaine and structurally similar compds. For structurally dissimilar uptake inhibitors, however, there was no significant correlation among potencies for stimulation of activity and affinity for displacement of [3H]WIN 35,428 binding. These findings provide evidence that cocaine analogs may bind to the dopamine transporter in a manner that is fundamentally different from that for structurally dissimilar uptake inhibitors.

ACCESSION NUMBER: 1994:645160 CAPLUS
DOCUMENT NUMBER: 121:245160
TITLE: Differential relationships among dopamine transporter affinities and stimulant potencies of various uptake inhibitors
AUTHOR(S): Izenwasser, Sari; Terry, Philip; Heller, Brett; Witkin, Jeffrey M.; Katz, Jonathan L.
CORPORATE SOURCE: Psychobiology Section, National Institute on Drug Abuse, Intramural Research Program, National Institutes of Health, P.O. Box 5180, Baltimore, MD, 21224, USA
SOURCE: European Journal of Pharmacology (1994), 263(3), 277-83
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 84 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

GI



II

AB Optically active 1-aryl-1,3-propanediol (I: X=F or H) is prepared by enzymic resolution of 1-aryl-1,3-diacetoxypropane (II: X is same as above; Ac=acetyl) with (immobilized) lipase. I are useful intermediates for fluoxetine or tomoxetine. Preparation of R-1-phenyl-1,3-propanediol from racemic 1-phenyl-1,3-diacetoxypropane with lipase PS immobilized on κ-carrageenan was shown.

ACCESSION NUMBER: 1994:555916 CAPLUS
DOCUMENT NUMBER: 121:155916
TITLE: Enzymic resolution of 1-aryl-1,3-diacetoxypropane
INVENTOR(S): Myazawa, Kazutoshi; Yoshida, Naoyuki; Sugiura, Mitsuyo; Koizumi, Yasuyuki
PATENT ASSIGNEE(S): Chisso Corp, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06125789	A2	19940510	JP 1992-300685	19921014
PRIORITY APPLN. INFO.:			JP 1992-300685	19921014

OTHER SOURCE(S): MARPAT 121:155916

L9 ANSWER 85 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Using radioligand binding assays and post-mortem normal human brain tissue, the authors obtained equilibrium dissociation consts. (Kds) for 17 antidepressants and two of their metabolites at histamine H1, muscarinic, α1-adrenergic, α2-adrenergic, dopamine D2, serotonin 5-HT1A, and serotonin 5-HT2 receptors. Several newer antidepressants were compared with older drugs. In addition, the authors studied some antimuscarinic, antiparkinson, antihistamine, and neuroleptic compds. at some of these receptors. For the antidepressants, classical tricyclic antidepressants were the most potent drugs at five of the seven receptors (all but α2-adrenergic and 5-HT1A receptors). The chlorophenylpiperazine derivative antidepressants (etoperidone, nefazodone, trazodone) were the most potent antidepressants at α2-adrenergic and 5-HT1A receptors. Of ten antihistamines tested, none was more potent than doxepin at histamine H1 receptors. At muscarinic receptors antidepressants and antihistamines had a range of potencies, which were mostly weaker than those for antimuscarinics. From the in vitro data, the authors expect adinazolam, bupropion, fluoxetine, sertraline, tomoxetine, and venlafaxine not to block any of these five receptors in vivo. An antidepressant's potency for blocking a specific receptor is predictive of certain side effects and drug-drug interactions. These studies can provide guidelines for the clinician in the choice of antidepressant.

ACCESSION NUMBER: 1994:449972 CAPLUS
DOCUMENT NUMBER: 121:49972
TITLE: Binding of antidepressants to human brain receptors: focus on newer generation compounds
AUTHOR(S): Cusack, Bernadette; Nelson, Albert; Richelson, Elliott
CORPORATE SOURCE: Dep. Res., Mayo Clin. Jacksonville, Jacksonville, FL, 32224, USA
SOURCE: Psychopharmacology (Berlin, Germany) (1994), 114(4), 559-65
CODEN: PSCHDL; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 86 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Narcolepsy is currently treated with antidepressants to control REM-related symptoms such as cataplexy and with amphetamine-like stimulants for the management of sleepiness. Both stimulant and antidepressant drugs presynaptically enhance monoaminergic transmission but both classes of compds. lack pharmacol. specificity. In order to determine which monoamine is selectively involved in the therapeutic effect of these compds., the authors examined the effects of selective monoamine uptake inhibitors and release enhancers on cataplexy using a canine model of the human disorder. A total of 14 compds. acting on the adrenergic (desipramine, nisoxetine, nortriptyline, tomoxetine, viloxazine), serotoninergic (fenfluramine, fluoxetine, indalpine, paroxetine, zimelidine) and dopaminergic (amfonelic acid, amineptine, bupropion, GBR 12909) systems were tested. Some addnl. compds. interesting clin. but with less pharmacol. selectivity, i.e., cocaine, dextroamphetamine, methylphenidate, nomifensine and pemoline, were also included in the study. All compds. affecting noradrenergic transmission completely suppressed canine cataplexy at low doses in all dogs tested, whereas compds. which predominantly modified serotoninergic and dopaminergic transmission were either inactive or partially active at high doses. The authors' results demonstrate the preferential involvement of adrenergic systems in the control of cataplexy and, presumably, REM sleep atonia. The authors' findings also demonstrate that canine narcolepsy is a useful tool in assessing the pharmacol. specificity of antidepressant drugs.

ACCESSION NUMBER: 1994:400675 CAPLUS
DOCUMENT NUMBER: 121:675
TITLE: Canine cataplexy is preferentially controlled by adrenergic mechanisms: evidence using monoamine selective uptake inhibitors and release enhancers
AUTHOR(S): Mignot, Emmanuel; Renaud, Alain; Nishino, Seiji; Arrigoni, Janis; Guilleminault, Christian; Dement, William C.
CORPORATE SOURCE: Sch. Med., Stanford Univ., Palo Alto, CA, 94304, USA
SOURCE: Psychopharmacology (Berlin, Germany) (1993), 113(1), 76-82
CODEN: PSCHDL; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 87 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB Eight White Carneau pigeons were trained to discriminate 1.0 or 1.7 mg/kg of cocaine from saline. A fixed number of consecutive key peck responses on one key after the administration of cocaine resulted in 4-s access to mixed grain. The same number of consecutive responses on the other key after saline also produced food. Different doses of cocaine and other drugs were tested to determine their ability to substitute (80% or more responding on the cocaine-appropriate key). The test drugs were selected to determine the selectivity of the cocaine discrimination in pigeons as well the role of different monoamines in mediating this behavioral effect. The drugs included other psychomotor stimulants, antidepressants, clonidine, yohimbine, other dopamine {(1-2-[bis(4-fluoro-phenyl)-methoxy]ethyl)4-3-phenylpropylpiperazine, GBR 12909) and serotonin (5-HT, sertraline) reuptake blockers, a D1 (SKF 75670), D2 (quinpirole), and 5-HT1A (8-hydroxy-2-(di-n-propylamino)tetralin, 8-PH-DPAT) agonist as well as the 5-HT3 antagonists, MDL 72222, LY 278584 and ondansetron. In addition, prazosin, an α1 adrenergic antagonist, SCH 23390, a D1 antagonist; raclopride, a D2 antagonist and 1-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl]piperazine (NAN-190), a putative 5-HT1A antagonist, were given in combination with cocaine to determine their ability to block the discriminative stimulus (DS) effects of cocaine, i.e., reduce drug-appropriate responding to 20% or less. The psychomotor stimulants, d-amphetamine and d-methamphetamine, completely substituted for cocaine and were similar in potency to each other and cocaine. The antidepressants l-deprenyl, imipramine, tomoxetine and bupropion also occasioned cocaine-appropriate responding. However, only partial substitution was seen with fluoxetine, clonidine, GBR 12909, quinpirole, SKF 75670 and 8-OH-DPAT. Responding occurred primarily on the saline-appropriate key after the administration of yohimbine, sertraline and the 5-HT3 antagonists. Prazosin, raclopride, SCH 23390 and NAN-190 blocked the DS effects of cocaine. Taken as a whole, these results indicate that the DS effects of cocaine are mediated not only by dopaminergic systems in the pigeon, as has been demonstrated in other species, but also at least in part by noradrenergic systems. Serotonin systems, in contrast, do not appear involved, although the results with fluoxetine, 8-OH-DPAT and NAN-190 warrant further investigation.
ACCESSION NUMBER: 1994:95445 CAPLUS
DOCUMENT NUMBER: 120:95445
TITLE: The discriminative stimulus effects of cocaine in pigeons
AUTHOR(S): Johanson, Chris Ellyn; Barrett, James E.
CORPORATE SOURCE: Dep. Psychiatry, Uniformed Serv. Univ. Health Sci., Bethesda, MD, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1993), 267(1), 1-8
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 88 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB The distribution of binding sites for the potent inhibitor of norepinephrine (NE) reuptake, [3H]tomoxetine, was examined in rat brain using quant. autoradiog. Scatchard anal. of [3H]tomoxetine-binding to slide-mounted sections of rat forebrain indicated that the ligand bound to 2 sites, a high-affinity site with a Kd of 0.29 nM and a lower-affinity site with a Kd of 16 nM. Pharmacol. characterization of this high-affinity site was consistent with labeling a NE-uptake site in brain. Autoradiog. localization of the binding sites for [3H]tomoxetine was performed at a ligand concentration of 1 nM representing the distribution of high-affinity sites. The radioligand bound with a distribution of binding sites that was consistent with the known distribution of NE-containing neurons. The highest levels of binding were seen in regions, such as the locus ceruleus, bed nucleus of the stria terminalis, anterior ventral nucleus of the thalamus and the paraventricular nucleus of the hypothalamus. Low levels were seen in regions such as the caudate-putamen, ventral tegmental area and zona reticulata of the substantia nigra, where NE-containing neurons have been reported to be low. Binding to all these sites was inhibited by 1 μM desipramine which produced autoradiograms with a uniform nonspecific binding. Apparently, low concns. of [3H]tomoxetine can be used to localize and characterize NE-binding sites.
ACCESSION NUMBER: 1993:618089 CAPLUS
DOCUMENT NUMBER: 119:218089
TITLE: Localization of rat brain binding sites for [3H]tomoxetine, an enantiomerically pure ligand for norepinephrine reuptake sites
AUTHOR(S): Gehlert, Donald R.; Gackenheimer, Susan L.; Robertson, David W.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Neuroscience Letters (1993), 157(2), 203-6
CODEN: NELED5; ISSN: 0304-3940
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 89 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB The effects of norepinephrine (NE) reuptake inhibition on NE release and contractile responses in lower urinary tract tissues were evaluated using tomoxetine, a selective NE reuptake inhibitor, and imipramine, a nonselective reuptake inhibitor. Although both compds. significantly increased K+-evoked release of NE from urethral fragments obtained from rabbits, tomoxetine was at least 10X more potent than imipramine. Tomoxetine significantly enhanced the effects of NE to contract rabbit urethral fragments and to relax carbachol contracted rabbit bladder smooth muscle. Imipramine suppressed the effects of NE on urethral tissue and was less potent than tomoxetine in enhancing bladder responses to NE. These presynaptic and postsynaptic effects of NE reuptake inhibition in lower urinary tract tissues may contribute to the efficacy of imipramine in treating incontinence and represent a new clin. utility for selective and more potent reuptake inhibitors, such as tomoxetine.
ACCESSION NUMBER: 1993:487042 CAPLUS
DOCUMENT NUMBER: 119:87042
TITLE: Alterations in potassium-evoked release of 3H-norepinephrine and contractile responses in urethral and bladder tissues induced by norepinephrine reuptake inhibition
AUTHOR(S): Foreman, M. M.; McNulty, A. M.
CORPORATE SOURCE: Lilly Corp. Cent., Lilly Res. Lab., Indianapolis, IN, 46285, USA
SOURCE: Life Sciences (1993), 53(3), 193-200
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 90 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB We determined the uptake blockade produced by eight new antidepressant drugs (etoperidone, femoxetine, lofepramine, nefazodone, paroxetine, sertraline, tomoxetine, and venlafaxine), two metabolites of newer antidepressants, and carbamazepine. Inhibitor consts. (Kis) for uptake blockade were obtained from competitive uptake studies with [3H]norepinephrine, [3H]5-hydroxytryptamine, and [3H]dopamine in rat brain synaptosomes prepared from hippocampus, frontal cortex, and striatum, resp. Among the newer compds., tomoxetine (Ki = 0.7 nM) and lofepramine (Ki = 1.9 nM) were potent and selective]3H]norepinephrine uptake blockers; paroxetine (Ki = 0.73 nM), sertraline (Ki = 3.4 nM), and femoxetine (Ki = 22 nM) potently and selectively inhibited [3H]5-hydroxytryptamine uptake. Although none of the drugs was potent for [3H]dopamine uptake blockade, sertraline was the most potent (Ki = 260 nM). These data are useful in predicting adverse effects and drug-drug interactions of antidepressants.
ACCESSION NUMBER: 1993:183305 CAPLUS
DOCUMENT NUMBER: 118:183305
TITLE: Blockade by newly-developed antidepressants of biogenic amine uptake into rat brain synaptosomes
AUTHOR(S): Bolden-Watson, C.; Richelson, E.
CORPORATE SOURCE: Mayo Clin., Jacksonville, FL, 32224, USA
SOURCE: Life Sciences (1993), 52(12), 1023-9
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 91 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A novel route for the synthesis of benzothiopyran and benzothiazepin ring systems along with the synthesis of optically pure, clin. effective drugs tomoxetine, fluoxetine and thiazesim is demonstrated.

ACCESSION NUMBER: 1993:101919 CAPLUS
DOCUMENT NUMBER: 118:101919
TITLE: A novel chemoenzymic enantioselective synthesis of some clinically effective CNS drugs and related compounds
AUTHOR(S): Kumar, Ashok; Ner, D. H.; Dike, Suneel
CORPORATE SOURCE: Alchemie Res. Cent., Thane, 400 601, India
SOURCE: Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1992), 31B(12), 803-9
CODEN: IJSBDB; ISSN: 0376-4699
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 118:101919

L9 ANSWER 92 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Alcs. are acylated in the presence of a vinyl ester or carboxylic acid ester and Pseudomonas lipase immobilized on a polystyrene resin. The chiral products can be used in synthesis of protease inhibitors, non-steroidal anti-inflammatory drugs, beta-blockers, and other drugs. Geraniol was incubated with the lipase immobilized on Amberlite XAD-2 and vinyl acetate. A quant. yield of geraniol acetate was obtained in 1 h. When the enzyme was not immobilized, the same yield required 50% more time. The stability of the enzyme was also increased by immobilization.

ACCESSION NUMBER: 1992:632211 CAPLUS
DOCUMENT NUMBER: 117:232211
TITLE: Acylation of alcohols with immobilized Pseudomonas lipase
INVENTOR(S): Schudok, Manfred; Fuelling, Gerd; Kretzschmar, Gerdhard
PATENT ASSIGNEE(S): Hoechst A.-G., Germany
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 492497	A2	19920701	EP 1991-121933	19911220
EP 492497	A3	19931020		
EP 492497	B1	19960828		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, NL				
CA 2058185	AA	19920625	CA 1991-2058185	19911220
AT 141950	E	19960915	AT 1991-121933	19911220
JP 04287689	A2	19921013	JP 1991-340796	19911224
JP 3117157	B2	20001211		
US 5387514	A	19950207	US 1993-173938	19931228
PRIORITY APPLN. INFO.:			DE 1990-4041777 A	19901224
			US 1991-806310 B1	19911213

OTHER SOURCE(S): MARPAT 117:232211

L9 ANSWER 93 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Tomoxetine is useful for treatment of lower urinary tract disorders, e.g. urinary incontinence, detrusor instability, and interstitial cystitis. The preferred dosage is 0.5-20 mg/kg orally, rectally, topically, or parenterally.

ACCESSION NUMBER: 1992:563878 CAPLUS
DOCUMENT NUMBER: 117:163878
TITLE: tomoxetine for treatment of lower urinary tract disorders
INVENTOR(S): Foreman, Mark Mortensen
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 501705	A1	19920902	EP 1992-301494	19920224
EP 501705	B1	19960515		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
CA 2061665	AA	19920826	CA 1992-2061665	19920221
CA 2061665	C	20020416		
AU 9211170	A1	19920827	AU 1992-11170	19920221
AU 642582	B2	19931021		
ZA 9201292	A	19930823	ZA 1992-1292	19920221
JP 05070343	A2	19930323	JP 1992-36029	19920224
JP 3222524	B2	20011029		
HU 62192	A2	19930428	HU 1992-602	19920224
HU 215122	B	19980928		
AT 137965	E	19960615	AT 1992-301494	19920224
US 5441985	A	19950815	US 1993-61335	19930513
PRIORITY APPLN. INFO.:			US 1991-660767 A	19910225

L9 ANSWER 94 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB The tricyclic antidepressant imipramine was established as a discriminative stimulus in pigeons at two doses (3.0 or 5.6 mg/kg). Because imipramine has multiple effects on different neurotransmitter systems, a range of compds. from several pharmacol. classes were tested for substitution. The tricyclic antidepressants desipramine, amitriptyline and doxepine, all of which block serotonin (5-HT) and norepinephrine (NE) reuptake, resulted in imipramine-key responding. The psychomotor stimulants cocaine and d-amphetamine also occasioned responding on the imipramine key, as did the NE reuptake inhibitor tomoxetine; nomifensine, which blocks the reuptake of both NE and dopamine (DA), also resulted in responding on the key correlated with imipramine injections. Bupropion, a DA reuptake inhibitor, resulted in drug key responding but substitution did not occur with another DA uptake inhibitor GBR 12909. The alpha-2 agonist clonidine, the 5-HT2 antagonist ritanserin or the 5-HT reuptake inhibitor fluoxetine also did not occasion drug-key responding. Drug-appropriate responding occurred in pigeons trained at the lower dose of imipramine with the 5-HT1A compds. 8-hydroxy-2-(di-n-propylamino)tetralin hydrobromide and gepirone; partial substitution occurred in pigeons trained with the higher dose of impramine. Substitution for the imipramine stimulus by gepirone, an antidepressant with actions mediated by the 5-HT1A receptor, as well as with 8-hydroxy-2-(di-n-propylamino)tetralin hydrobromide, suggests that imipramine may have effects at this receptor site and confirms reports that compds. active at this receptor may have antidepressant activity. This appears to be the first report of the successful long-term establishment of imipramine as a discriminative stimulus without the development of toxicity. These results indicate that the discriminative stimulus effects of imipramine are complex and involve at least NE reuptake and a specific 5-HT receptor subtype (1A). Generalization to the imipramine stimulus by cocaine and d-amphetamine also suggests that further analyses of these drugs as discriminative stimuli, with particular attention to the possible role of the 5-HT1A receptor and NE systems, may aid in clarifying their neurochem. and behavioral actions as abused drugs.

ACCESSION NUMBER: 1992:76250 CAPLUS
DOCUMENT NUMBER: 116:76250
TITLE: Imipramine as a discriminative stimulus
AUTHOR(S): Zhang, L.; Barrett, J. E.
CORPORATE SOURCE: Dep. Psychiatry, Uniformed Serv. Univ. Health Sci., Bethesda, MD, 20814-4799, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1991), 259(3), 1088-93
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 95 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Rhesus monkeys trained in a two-lever, food-reinforced paradigm to discriminate cocaine (0.2 or 0.4 mg/kg, i.m.) from saline, received injections of cocaine (0.025-0.40 mg/kg, i.v. or i.m.) or various direct and indirect acting agonists (i.v.). Administration of cocaine resulted in a dose-related increase in the percentage of responses that occurred on the drug-appropriate lever. The indirect dopamine agonists GBR 12909 (0.2-1.6 mg/kg), mazindol (0.025-0.4 mg/kg), nomifensine (0.025-0.2 mg/kg) and bupropion (0.1-1.6 mg/kg) each produced dose-related increase in cocaine-appropriate responding, with complete substitution for cocaine achieved at the highest doses of each drug. In contrast, the norepinephrine re-uptake blockers tomoxetine (0.8-6.4 mg/kg) and nisoxetine (0.4-1.6 mg/kg), the serotonin re-uptake blocker fluoxetine (1.6-12.8 mg/kg), the D1 agonist SKF 38393 (3.2-12.8 mg/kg) and the D2 agonist quinpirole (0.05-0.2 mg/kg) failed to engender cocaine-appropriate responding. Administration of the D1 antagonist SCH 23390 (0.05-0.2 mg/kg, i.m.) 20 min before cocaine resulted in a 4- to 8-fold parallel shift to the right in the cocaine dose-response function. Similarly, the D2 antagonist haloperidol (0.003-0.012 mg/kg, i.m.) produced at least 2-fold shift to the right in the cocaine dose-response function. The results indicate that blockade of dopamine re-uptake is sufficient to mimic the cocaine discriminative stimulus and suggest that stimulation of either D1 or D2 receptors is necessary but not sufficient for the expression of the discriminative stimulus effects of cocaine.

ACCESSION NUMBER: 1990:526451 CAPLUS
DOCUMENT NUMBER: 113:126451
TITLE: Pharmacological characterization of the discriminative stimulus effects of cocaine in rhesus monkeys
AUTHOR(S): Kleven, Mark S.; Anthony, Elizabeth W.; Woolverton, William L.
CORPORATE SOURCE: Dep. Pharmacol. Physiol. Sci., Univ. Chicago, Chicago, IL, 60637, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1990), 254(1), 312-17
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 96 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB Optically active alcs. R1R2CHOH [I; R1 = (halogen substituted) C1-18 alkyl, C8-10 cycloalkyl; R2 = epoxy-C1-5 alkyl; (substituted) C1-10 alkyl, C2-10 alkenyl or alkynyl, C3-8 cycloalkenyl] are produced from the racemic alc. and a vinyl ester CH2:CHR3OC(:O)R4 [II; R3 = H, Me; R4 = H, (halogen-substituted) C1-8 alkyl, Ph, C1-3 alkoxy-C1-4 alkyl; R3,R4 together = alkenylene] with a lipase from swine liver or pancreas, or from microorganisms such as Candida, Mucor, etc. The optically active alcs. may be used to prepare nonsteroidal anti-inflammatory drugs, β-blockers, bronchospasmolytics, antimycotics, pyrethroids, prostaglandins, carbohydrates, etc. Vinyl acetate or vinyl chloroacetate and 31 different alcs. were incubated with Lipase P or FP to prepare optically active alcs. in yields varying from 28-98% and enantiomeric excess of 23-98%.

ACCESSION NUMBER: 1990:137568 CAPLUS
DOCUMENT NUMBER: 112:137568
TITLE: Process for the enzymatic resolution of racemic alcohols with/in vinyl esters by transesterification
INVENTOR(S): Keller, Reinhold; Holla, Wolfgang; Fuelling, Gerd
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 321918	A2	19890628	EP 1988-121274	19881220
EP 321918	A3	19901003		
EP 321918	B1	19940323		
EP 321918	B2	19990414		
R: BE, CH, DE, FR, GB, IT, LI, NL				
DE 3743824	A1	19890706	DE 1987-3743824	19871223
DE 3743824	C2	19970306		
US 4963492	A	19901016	US 1988-287371	19881221
JP 01202296	A2	19890815	JP 1988-322246	19881222
JP 07002118	B4	19950118		

PRIORITY APPLN. INFO.: DE 1987-3743824 A 19871223

OTHER SOURCE(S): MARPAT 112:137568

L9 ANSWER 97 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

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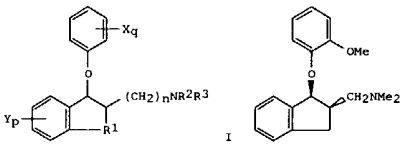

AB Title compds. I [R1 = C1-3 alkylene; n, p, q = 0-2; X, Y = C1-6 alkyl or alkoxy, OH, CF3, halo; or (X)2, (Y)2 = OCH2O; R2, R3 = H, C1-6 alkyl, aralkyl; or NR2R3 = pyrrolidino, morpholino, piperidino, piperazino, 4-methylpiperazino] were prepared as antidepressants (no data). In addition, administering uptake inhibitors of both norepinephrine and serotonin produced synergistic down-regulation of β-adrenergic receptors in rats. Reduction of 2,3-dihydro-2-(N,N-dimethylaminomethyl)-1H-inden-1-one-HCl by L-Selectride in THF gave 48% of the cis alc., which was etherified with 2-FC6H4OMe using NaH in Me2SO to give cis-dihydro(methoxyphenoxy)dimethyli ndenemethanamine II. In a sep. rat experiment combined treatment with desipramine (5 mg/kg, i.p.) and fluoxetine (10 mg/kg, i.p.) for 14 days down-regulated cortical β-adrenergic receptor number to 64% of control, vs. only 86% and 91% by the resp. drugs alone.

ACCESSION NUMBER: 1989:533804 CAPLUS
DOCUMENT NUMBER: 111:133804
TITLE: Preparation and formulation of (aryloxy)indanamines and related compounds useful as antidepressants and as inhibitors of synaptic norepinephrine and serotonin uptake
INVENTOR(S): Freedman, Jules; Dudley, Mark W.
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 303961	A2	19890222	EP 1988-112996	19880810
EP 303961	A3	19890517		
EP 303961	B1	19940413		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8805824	A	19890426	ZA 1988-5824	19880808
CA 1327795	A1	19940315	CA 1988-574102	19880808

L9 ANSWER 97 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AU 8820579	A1	19890216	AU 1988-20579	19880809
AU 606444	B2	19910207		
AT 104269	E	19940415	AT 1988-112996	19880810
ES 2054747	T3	19940816	ES 1988-112996	19880810
FI 8803739	A	19890215	FI 1988-3739	19880811
FI 91852	B	19940513		
FI 91852	C	19940825		
JP 01066151	A2	19890313	JP 1988-199045	19880811
JP 2650045	B2	19970903		
IL 87412	A1	19950526	IL 1988-87412	19880811
DK 8804546	A	19890215	DK 1988-4546	19880812
NO 8803595	A	19890215	NO 1988-3595	19880812
NO 167913	B	19910916		
NO 167913	C	19911227		
HU 51593	A2	19900528	HU 1988-4347	19880812
HU 204504	B	19920128		
CN 1033043	A	19890524	CN 1988-106476	19880813
CN 1021323	B	19930623		
KR 126137	B1	19971226	KR 1988-10350	19880813
US 5149714	A	19920922	US 1990-569259	19900815
US 5561152	A	19961001	US 1994-350236	19941206
US 5880120	A	19990309	US 1997-937224	19970911
US 6136803	A	20001024	US 1998-209200	19981210

PRIORITY APPLN. INFO.:

US 1987-85665	A	19870814
EP 1988-112996	A	19880810
US 1988-287517	B3	19881219
US 1989-296474	B1	19890112
US 1989-401518	B2	19890829
US 1989-434665	B1	19891113
US 1990-569259	A1	19900815
US 1991-762050	B1	19910918
US 1992-820475	B1	19920114
US 1992-855125	B1	19920318
US 1992-979357	B1	19921120
US 1993-46104	B1	19930408
US 1993-133829	B1	19931007
US 1993-170437	B1	19931220
US 1994-278697	B1	19940721
US 1994-294774	B1	19940823
US 1995-440511	B1	19950512
US 1996-733901	B1	19961018

L9 ANSWER 97 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

	US 1997-937224 A3 19970911
OTHER SOURCE(S):	MARPAT 111:133804

L9 ANSWER 98 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

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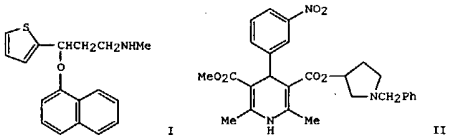

I II

AB HPLC methods were developed to sep. some CNS drugs, both indirectly after diastereomer formation, and directly using chiral stationary phases. Some examples are: resolution of fluoxetine as mandelic acid derivative on a H2 column; resolution and determination of I as Mosher's acid derivative on a NH2 column or the acetylate I derivative on a Cyclobond I column; chromatog. of tomoxetine spiked with its (+)-isomer on a Cyclobond I column after acetylation; and chiral separation of the Ca channel blocker II on an α1-acid glycoprotein column.

ACCESSION NUMBER:	1988:535063 CAPLUS
DOCUMENT NUMBER:	109:135063
TITLE:	Practical considerations for chiral separations of pharmaceutical compounds
AUTHOR(S):	Bopp, Ronald J.; Kennedy, Joseph H.
CORPORATE SOURCE:	Lilly Corp. Cent., Eli Lilly Co., Indianapolis, IN, 46285, USA
SOURCE:	LC-GC (1988), 6(6), 514, 516, 518, 520, 522 CODEN: LCGCE7; ISSN: 0888-9090
DOCUMENT TYPE:	Journal
LANGUAGE:	English

L9 ANSWER 99 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB A polemic. The comparison between R-(-)-tomoxetine (R-(-)-I) and R-(-)-noradrenaline (R-(-)-II) as presented by Wong et al (ibid. 1982, 222, 61-65) is not valid due to the change in priorities in numbering the groups attached to the chiral centers of these 2 mols. Thus the biol. relevant R-(-)-isomer of II has the same configuration as the less active S-(+)-isomer of I and S-(-)-isomer of nisoxetine.

ACCESSION NUMBER:	1988:16321 CAPLUS
DOCUMENT NUMBER:	108:16321
TITLE:	Tomoxetine and the stereoselectivity of drug action
AUTHOR(S):	Oberlender, Robert; Nichols, David E.; Ramachandran, P. V.; Srebnik, Morris; Brown, H. C.; Wetherill, R. B.
CORPORATE SOURCE:	Sch. Pharm. Pharmacal Sci., Purdue Univ., West Lafayette, IN, 47907, USA
SOURCE:	Journal of Pharmacy and Pharmacology (1987), 39(12), 1055-6 CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE:	Journal
LANGUAGE:	English

L9 ANSWER 100 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN

AB (±)-2-MeC6H4OCH(Ph)CH2CH2NHMe [(±)-I], the racemate of the antidepressant tomoxetine [(-)-I], is prepared by reacting (+)-I with RM (R = alkyl, alkylamide; M = alkali metal) in MeOCH2CH2OMe or THF under inert conditions. Thus, BuLi in hexane was added over 5 min to (+)-I in THF at 17-22° and the mixture stirred for .apprx.3.5 h to give 97% (±)-I. Resolution of (±)-I gave 49% (-)-I.L-(+)-mandelic acid, which was hydrolyzed by NaOH in Et2O and acidified to give 62.7% (-)-I.

ACCESSION NUMBER:	1986:626035 CAPLUS
DOCUMENT NUMBER:	105:226035
TITLE:	Racemization of tomoxetine enantiomer
INVENTOR(S):	Misner, Jerry Wayne
PATENT ASSIGNEE(S):	Eli Lilly and Co., USA
SOURCE:	Eur. Pat. Appl., 22 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 193405	A1	19860903	EP 1986-301417	19860227
EP 193405	B1	19890308		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4777291	A	19881011	US 1985-706373	19850227
CA 1269997	A1	19900605	CA 1986-502597	19860225
JP 61210059	A2	19860918	JP 1986-42792	19860226
HU 42055	A2	19870629	HU 1986-815	19860226
HU 196586	B	19881228		
AT 41144	E	19890315	AT 1986-301417	19860227
PRIORITY APPLN. INFO.:			US 1985-706373 A	19850227
			EP 1986-301417 A	19860227

L9 ANSWER 101 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB Antidepressants interacted competitively with putative adenosine transport
sites and adenosine receptors of rat brain membranes in a study of the abilities of 12 antidepressants to compete with 3H-labeled nitrobenzylthioinosine [38048-32-7] binding to putative adenosine transport sites and with 3H-labeled cyclohexyladenosine (II) [36396-99-3]
binding to adenosine receptors. Chronic treatment of rats with doxepin [1668-19-5] increased the number of adenosine receptors (as determined by II
binding to receptor sites of the brain). Brain adenosine deaminase [9026-93-1] was not affected by 5 of the antidepressants (clorgyline [17780-72-2], amitriptyline [50-48-6], zimelidine [56775-88-3], and doxepin).

ACCESSION NUMBER: 1986:527404 CAPLUS
DOCUMENT NUMBER: 105:127404
TITLE: Antidepressant competition for adenosine binding sites
and chronic doxepin induced increases in adenosine receptors
AUTHOR(S): Lewis, J. L.; Geiger, J. D.
CORPORATE SOURCE: Fac. Med., Univ. Manitoba, Winnipeg, MB, R3E 0W3, Can.
SOURCE: Proceedings of the Western Pharmacology Society (1986), 29, 265-9
CODEN: PWPSA8; ISSN: 0083-8969
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 102 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB A pharmacokinetic profile of tomoxetine **[83015-26-3]**, a selective norepinephrine uptake inhibitor, was developed in human volunteers following single and multiple oral administrations. Following the administration of a single 90-mg oral dose of tomoxetine to 4 normal volunteers, the plasma half-life was 4.3 h. Mean plasma clearance was 0.60 L/kg/h, and the mean volume of distribution was 3.7 L/kg. When 2 doses
per day (20 mg and 40 mg) were administered for 7 days, the data appeared to have bimodal distribution. The mean plasma half-life determined following
the last dose was 4.6 h in 5 subjects. The other 2 subjects, 1 at each dose level, demonstrated accumulation of tomoxetine occurring from the first to last dose where tomoxetine disappeared from plasma with a mean half-life of 19 h.

ACCESSION NUMBER: 1985:515611 CAPLUS
DOCUMENT NUMBER: 103:115611
TITLE: Single-dose and steady-state pharmacokinetics of tomoxetine in normal subjects
AUTHOR(S): Farid, Nagy A.; Bergstrom, Richard F.; Ziege, Edgar A.; Parli, C. John; Lemberger, Louis
CORPORATE SOURCE: Lilly Lab. Clin. Res., Eli Lilly Co., Indianapolis, IN, USA
SOURCE: Journal of Clinical Pharmacology (1985), 25(4), 296-301
CODEN: JCPCBR; ISSN: 0091-2700
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 103 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
AB The effects of daily administration to rats of desipramine [50-47-5], talsupram [21489-20-3], tomoxetine **[83015-26-3]**, maprotiline [10262-69-8], nomifensine maleate [32795-47-4] mianserin [24219-97-4] and citalopram [59729-33-8] (each 10 mg kg-1 day-1) for 4 wk on [3H]dihydroalprenolol ([3H]DHA) binding in the cerebral cortex and on the noradrenaline [51-41-2]-sensitive adenylate cyclase [9012-42-4] in the limbic forebrain were determined. Of these compds., only desipramine reduced
[3H]DHA binding and attenuated the cAMP [60-92-4] response. Two selective noradrenaline uptake inhibitors, talsupram and tomoxetine each reduced the cAMP response but without affecting [3H]DHA binding. The other drugs lacked effect on both measures indicating (except for citalopram) that reduction in sensitivity of β-adrenoceptors and of the noradrenaline-sensitive cAMP response might not be a simple consequence of
noradrenaline uptake inhibition. The lack of effect of citalopram on the sensitivity of the β-adrenoceptor system suggests that antidepressants with selective 5-HT [50-67-9] uptake inhibitory properties owe their antidepressant activity to other mechanisms.

ACCESSION NUMBER: 1985:160303 CAPLUS
DOCUMENT NUMBER: 102:160303
TITLE: Effects of some atypical antidepressants on β-adrenoceptor binding and adenylate cyclase activity in the rat forebrain
AUTHOR(S): Garcha, Gurbakhsh; Smokcum, Roger W. J.; Stephenson, John D.; Weeramanthri, Tara B.
CORPORATE SOURCE: Dep. Pharmacol., Inst. Psychiatry, London, SE5 8AF, UK
SOURCE: European Journal of Pharmacology (1985), 108(1), 1-7
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 104 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
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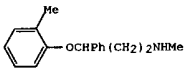
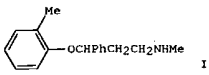


I

AB Tomoxetine (I) **[83015-26-3]** was administered in single oral doses up to 90 mg to healthy normal volunteers. In addition, normal human
subjects received either 20 or 40 mg of tomoxetine twice a day (b.i.d.) for 1 wk to evaluate the safety and pharmacol. activity of the compound in
humans. At these doses, no serious drug-related adverse effects were encountered. Activity of the compound at the lower dose (20 mg b.i.d.) was
evaluated by examining changes in the pressor responses to infused norepinephrine and tyramine and by determining [3H]serotonin uptake in platelets
harvested from subjects receiving the compound. Pressor sensitivity to norepinephrine was increased by 261% of control, and pressor sensitivity to tyramine was decreased by 51% of control during treatment. Changes in the pressor sensitivity to norepinephrine in individual subjects were pos.
correlated with drug levels. There were no statistically significant changes in platelet [3H]serotonin uptake. Apparently, tomoxetine selectively inhibits norepinephrine uptake in humans at doses which are clin. well tolerated and tomoxetine has potential clin. use as an antidepressant.

ACCESSION NUMBER: 1985:106154 CAPLUS
DOCUMENT NUMBER: 102:106154
TITLE: Clinical pharmacology of tomoxetine, a potential antidepressant
AUTHOR(S): Zerbe, Robert L.; Rowe, Howard; Enas, Gregory G.; Wong, David; Farid, Nagy; Lemberger, Louis
CORPORATE SOURCE: Lilly Lab. Clin. Res., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1985), 232(1), 139-43
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 105 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
GI

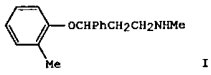


I

AB Tomoxetine (I) **[83015-26-3]**, a potential antidepressant drug, antagonized the α-methyl-m-tyrosine-induced depletion of hypothalamic epinephrine [51-43-4] and norepinephrine [51-41-2] in rats.
The findings suggest that tomoxetine, like several uptake-inhibiting antidepressant drugs, inhibits uptake into epinephrine neurons as well as into norepinephrine neurons in brain.

ACCESSION NUMBER: 1983:533530 CAPLUS
DOCUMENT NUMBER: 99:133530
TITLE: Antagonism by tomoxetine of the depletion of norepinephrine and epinephrine in rat brain by α-methyl-m-tyrosine
AUTHOR(S): Fuller, Ray W.; Hemrick-Luecke, Susan K.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Research Communications in Chemical Pathology and Pharmacology (1983), 41(1), 169-72
CODEN: RCOCB8; ISSN: 0034-5164
DOCUMENT TYPE: Journal
LANGUAGE: English

L9 ANSWER 106 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I

AB The levorotatory form of amine I was prepared, and (−)-I·HCl (II) exhibited antidepressant activity (formulations are given). Thus, 2-MeC6H4OCHPhCH2CH2NMe2 was converted to 2-MeC6H4OCHPhCH2CH2NMeCO2Ph, the latter was deacylated to racemic I·HCl, and resolution with L(+)-mandelic acid gave II.

ACCESSION NUMBER: 1982:615718 CAPLUS
DOCUMENT NUMBER: 97:215718
TITLE: 3-Aryloxy-3-phenylpropylamines
INVENTOR(S): Foster, Bennie Joe; Lavagnino, Edward Ralph
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 52492	A1	19820526	EP 1981-305387	19811113
EP 52492	B1	19840229		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
FI 8103589	A	19820515	FI 1981-3589	19811112
FI 77018	B	19880930		
FI 77018	C	19890110		
AU 8177427	A1	19820520	AU 1981-77427	19811112
AU 540707	B2	19841129		
ZA 8107863	A	19830629	ZA 1981-7863	19811112
RO 83309	P	19840221	RO 1981-105785	19811112
CA 1181430	A1	19850122	CA 1981-389954	19811112
DK 8105027	A	19820515	DK 1981-5027	19811113
DK 161887	B	19910826		
DK 161887	C	19920316		
GB 2087883	A	19820603	GB 1981-34282	19811113
JP 57114555	A2	19820716	JP 1981-182953	19811113
JP 03069885	B4	19911105		
ES 507142	A1	19820816	ES 1981-507142	19811113
DD 201139	C	19830706	DD 1981-234837	19811113
SU 1068034	A3	19840115	SU 1981-3355735	19811113
AT 6422	E	19840315	AT 1981-305387	19811113
HU 30622	O	19840328	HU 1981-3411	19811113
HU 185475	B	19850228		
CS 227019	P	19840416	CS 1981-8359	19811113
HU 32779	O	19840928	HU 1983-4481	19811113
IL 64288	A1	19850430	IL 1981-64288	19811115
JP 03007250	A2	19910114	JP 1990-147166	19900605
JP 04006698	B4	19920206		
JP 03007251	A2	19910114	JP 1990-147167	19900605

L9 ANSWER 106 OF 106 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

JP 04006699	B4	19920206	
PRIORITY APPLN. INFO.:		US 1980-206498	A 19801114
		EP 1981-305387	A 19811113

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Connecting via Winsock to STN



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PASSWORD:
 * * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 18:10:12 ON 06 DEC 2004
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COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     304.74     312.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                     -76.30     -76.30

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     FILE 'CAPLUS' ENTERED AT 17:52:29 ON 06 DEC 2004
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L5             3 S 83015-26-3D/RN
L6           109 S L4 OR L5
L7        143300 S SEX?
L8             3 S L6 AND L7
L9           106 S L6 NOT L8

=> s norephinephrine
L10          131 NOREPHINEPHRINE

=> s l10 and l7
L11            3 L10 AND L7

=> d l11 1-3 abs ibib
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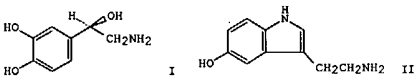
L11 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

AB In the present experiment, 6-OHDA was infused directly into the olfactory bulb (OB) to produce a localized neurotoxic lesion. Habituation/dishabituation behavioral tests were then conducted to measure recognition responses to chemical cues (urine as a stimulus) and to social stimuli (ovariectomized rat as a stimulus). Infusion of 6-OHDA resulted in a near complete depletion of OB-norepinephrine (NE), whereas it had little effect (15% reduction) on OB dopamine (DA) contents. Nor were any significant effects on hypothalamic, hippocampal, olfactory tubercle, and corpus striatal NE and DA contents observed Behaviorally, dishabituation responses to chemical cues were greatly impaired, however there was relatively little effect on social behavior dishabituation responses. These results demonstrate that 6-OHDA can be used to produce a near complete but localized depletion of OB-NE. This treatment impairs dishabituation responses to chemical cues but not social stimuli indicating that OB-NE appears necessary for processing of chemical cue, but not social memory recognition process.

ACCESSION NUMBER: 1993:596325 CAPLUS
DOCUMENT NUMBER: 119:196325
TITLE: Depletion of olfactory bulb norepinephrine by 6-OHDA disrupts chemical cue but not social recognition responses in male rats
AUTHOR(S): Guan, Xiaobin; Blank, James; Dluzen, Dean
CORPORATE SOURCE: Department of Anatomy, Northeastern Ohio Universities, College of Medicine, Rootstown, OH, 44272, USA
SOURCE: Brain Research (1993), 622(1-2), 51-7
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

L11 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

GI



I II

AB In brain synaptosomes from inbred mice (C57 strain) both noradrenaline (I) [51-41-2] and serotonin (II) [50-67-9] uptake was characterized by a high level of homogeneity with no variance with respect to hypothetical fluctuations in the methods used to measure such uptake, suggesting that interindividual differences found in uptake are not due to poor reliability in tech. procedures. In rats I uptake was affected by interindividual differences in synaptosomal prepns. as well as **sex** of the animal. Synaptosomes from male rats incorporated less I than did those from females.

ACCESSION NUMBER: 1979:551743 CAPLUS
DOCUMENT NUMBER: 91:151743
TITLE: Multivariate approaches applied to studies of **norephinephrine** and serotonin in uptake
AUTHOR(S): Sacchetti, E.; Allaria, E.; Conte, G.; De Rosa, A.; Griffi, P. G.; Taroni, P. L.; Resele, L.; Smeraldi, E.
CORPORATE SOURCE: Med. Sch., Milan Univ., Milan, Italy
SOURCE: Developments in Psychiatry (1979), Volume Date 1978, 2(Biol. Psychiatry Today, Vol. A), 137-41
CODEN: DPSYDX; ISSN: 0166-2481
DOCUMENT TYPE: Journal
LANGUAGE: English

L11 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

AB Castration of rats immediately after birth, which induces a permanent femininization of reproductive function, resulted in a marked reduction in the weight and total organ content of norepinephrine in the vasa deferentia as measured before and after **sexual** maturation. The norepinephrine fall was .apprx.3-fold greater than after castration of adult animals. Androgenization of female rats by a single injection of testosterone propionate on the 5th day post partum did not affect uterine weight, but significantly lowered total organ content of norepinephrine when measured before and after **sexual** maturation. Thus, the vasa deferentia and uterus contain a population of adrenergic nerves, probably identical with or part of the system of short adrenergic neurons that constitute a sep. target system for those humoral factors which determine the pattern of development of the reproductive tract by influencing the early differentiation of the hypothalamus.

ACCESSION NUMBER: 1974:518002 CAPLUS
DOCUMENT NUMBER: 81:118002
TITLE: Consequence of neonatal androgenization and castration for future levels of norepinephrine transmitter in uterus and vas deferens of the rat
AUTHOR(S): Broberg, A.; Nybell, G.; Owman, Ch.; Rosengren, E.; Sjoberg, N. O.
CORPORATE SOURCE: Dep. Histol., Univ. Lund, Lund, Swed.
SOURCE: Neuroendocrinology (1974), 15(5), 308-12
CODEN: NUNDAJ; ISSN: 0028-3835
DOCUMENT TYPE: Journal
LANGUAGE: English

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          4900 "TRANSPORTS"
        634978 "TRANSPORT"
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        458835 "INHIBITOR"
        476211 "INHIBITORS"
        736009 "INHIBITOR"
                 ("INHIBITOR" OR "INHIBITORS")
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     FILE 'CAPLUS' ENTERED AT 17:52:29 ON 06 DEC 2004
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L3          50 S ATOMOXETINE
L4         107 S 83015-26-3/RN
L5           3 S 83015-26-3D/RN
L6         109 S L4 OR L5
L7      143300 S SEX?
L8           3 S L6 AND L7
L9         106 S L6 NOT L8
L10        131 S NOREPHINEPHRINE
L11          3 S L10 AND L7
L12          0 S "NOREPHINEPHRINE TRANSPORT INHIBITOR"

=> s noradrenergic
        11336 NORADRENERGIC
            1 NORADRENERGICS
L13     11336 NORADRENERGIC
                 (NORADRENERGIC OR NORADRENERGICS)

=> s l13 and l7
L14       287 L13 AND L7

=> s l14 and l10
L15          1 L14 AND L10

=> d l15 abs ibib
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L15 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN

AB In the present experiment, 6-OHDA was infused directly into the olfactory bulb (OB) to produce a localized neurotoxic lesion. Habituation/dishabituation behavioral tests were then conducted to measure recognition responses to chemical cues (urine as a stimulus) and to social stimuli (ovariectomized rat as a stimulus). Infusion of 6-OHDA resulted in a near complete depletion of OB-norepinephrine (NE), whereas it had little effect (15% reduction) on OB dopamine (DA) contents. Nor were any significant effects on hypothalamic, hippocampal, olfactory tubercle, and corpus striatal NE and DA contents observed Behaviorally, dishabituation responses to chemical cues were greatly impaired, however there was relatively little effect on social behavior dishabituation responses. These results demonstrate that 6-OHDA can be used to produce a near complete but localized depletion of OB-NE. This treatment impairs dishabituation responses to chemical cues but not social stimuli indicating that OB-NE appears necessary for processing of chemical cue, but not social memory recognition process.

ACCESSION NUMBER: 1993:596325 CAPLUS
DOCUMENT NUMBER: 119:196325
TITLE: Depletion of olfactory bulb norepinephrine by 6-OHDA disrupts chemical cue but not social recognition responses in male rats
AUTHOR(S): Guan, Xiaobin; Blank, James; Dluzen, Dean
CORPORATE SOURCE: Department of Anatomy, Northeastern Ohio Universities, College of Medicine, Rootstown, OH, 44272, USA
SOURCE: Brain Research (1993), 622(1-2), 51-7
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

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     FILE 'REGISTRY' ENTERED AT 17:50:54 ON 06 DEC 2004
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     FILE 'CAPLUS' ENTERED AT 17:52:29 ON 06 DEC 2004
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L7        143300 S SEX?
L8             3 S L6 AND L7
L9           106 S L6 NOT L8
L10          131 S NOREPHINEPHRINE
L11            3 S L10 AND L7
L12            0 S "NOREPHINEPHRINE TRANSPORT INHIBITOR"
L13        11336 S NORADRENERGIC
L14          287 S L13 AND L7
L15            1 S L14 AND L10

=> s l10 not l11
L16          128 L10 NOT L11

=> d l16 1-128 abs ibib
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L16 ANSWER 1 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB The antidepressants, reboxetine and citalopram, were used in conjunction with voluntary phys. exercise (wheel running) in order to assess the contribution of noradrenergic and serotonergic activation to enhancements in hippocampal brain-derived neurotrophic factor (BDNF) expression resulting from antidepressant treatment and exercise. Reboxetine (40 mg/kg/day), citalopram (10 mg/kg/day), voluntary phys. activity, and the combination of antidepressants with exercise were applied to rats for a range of treatment intervals (2 to 14 days). Hippocampal BDNF transcription levels (full-length BDNF, as well as exons I-IV) were then assessed via in situ hybridization.Reboxetine treatment led to a rapid (evident at 2 days) enhancement in BDNF transcription in several hippocampal regions. This increase was also observed when reboxetine treatment was combined with voluntary phys. activity for 2 wk. Treatment with citalopram led to an increase in BDNF mRNA in only one hippocampal region (CA2) after short-term (2 days) treatment, and when combined with exercise, increased BDNF mRNA in the CA4 and dentate gyrus after 2 wk. As reported in previous studies, voluntary phys. activity enhanced BDNF transcription in several hippocampal areas, both on its own and in combination with antidepressant treatments. Examination of the levels of individual BDNF transcript variants influenced by each of these antidepressants revealed distinct patterns of expression in response to the various treatments, and showed that exercise-plus-antidepressant produced significant changes where antidepressant alone failed. Overall, treatment with the **norephinephrine**-selective antidepressant, reboxetine, in combination with exercise, led to both rapid and sustained increases in hippocampal BDNF mRNA expression. The serotonergic agent, citalopram, appeared to require longer treatment intervals in order to influence BDNF expression pos.Neuropsychopharmacol. (2004) 29, 2189-2199, advance online publication, 16 June 2004;.

ACCESSION NUMBER: 2004:1005087 CAPLUS
TITLE: Hippocampal Brain-Derived Neurotrophic Factor Expression Following Treatment with Reboxetine, Citalopram, and Physical Exercise
AUTHOR(S): Russo-Neustadt, Amelia A.; Alejandre, Hilda; Garcia, Celithelma; Ivy, Autumn S.; Chen, Michael J.
CORPORATE SOURCE: Department of Biological Sciences, California State University, Los Angeles, CA, USA
SOURCE: Neuropsychopharmacology (2004), 29(12), 2189-2199
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 2 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB In August of 2001, the largest known installation of a phased temperature anaerobic process at a 60-MDG wastewater treatment plant was placed into operation. The facility met the time and temperature requirement for Class A biosolids. Testing of the biosolids following thermophillic/anaerobic digestion followed by mesophilic/anaerobic digestion revealed no detectable levels of fecal coliform bacteria in the treated biosolids. However, subsequent testing of the biosolids following dewatering by high solid centrifugation revealed high levels of fecal coliform bacteria. These biosolids, following high solid centrifugation, did not meet Class B requirements. This study indicated a very serious reactivation of fecal coliform bacteria following high solid centrifugation. Fifty-three percent of the fecal coliforms isolated were identified as Escherichia coli with two of the isolated organisms identified as E. coli O157:H7. E. coli O157:H7 has been shown to be capable of formation of an autoinducer in the presence of **norephinephrine**. The autoinducer triggers the growth of gram-neg. bacteria or the conversion of gram-neg. bacteria such as fecal coliforms from a non-culturable to culturable state. It is, therefore, hypothesized that the presence of E. coli O157:H7 may be involved in the reactivation of fecal coliform bacteria.

ACCESSION NUMBER: 2004:881666 CAPLUS
TITLE: Reactivation of fecal coliforms after anaerobic digestion and dewatering
AUTHOR(S): Hendrickson, Donald A.; Denard, Dave; Farrell, Joseph; Higgins, Matt
CORPORATE SOURCE: Hoosier Microbiological Laboratory, Muncie, IN, 47303, USA
SOURCE: WEF/WEAU Residuals and Biosolids Management Conference & Exhibition, 18th, Salt Lake City, UT, United States, Feb. 22-25, 2004 (2004), 908-916. Water Environment Federation: Alexandria, Va.
CODEN: 69FWM4
DOCUMENT TYPE: Conference; (computer optical disk)
LANGUAGE: English
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Both diabetes (db/db) and obese (ob/ob) genotype mutations induce a hyperglycemic-hyperinsulinemic endometabolic state in C57BL mice, manifesting a type II NIDDM diabetes-obesity syndrome (DOS) in these leptin ligand/receptor-deficient models. The severity of the DOS induced by these single gene, homozygous-recessive mutations may be moderated by the background genome on which the mutation is expressed. The current studies define the phenotypic, systemic, cytochem. and cellular metabolic responses to db/db and ob/ob mutation expression when modified by /KsJ (severe DOS expression) or /6 (modified DOS expression) background strain influences as compared to littermate control (+/) indexes. Both db/db and ob/ob mutations induced dramatic increases in body wts., blood glucose and serum insulin concns. relative to +/ indexes when expressed on either the C57BL/KsJ (-/KsJ) or C57BL/6 (-/6) backgrounds. However, the -/KsJ background enhanced the severity of expression of these DOS indexes relative to the -/6 strain. Similarly, the -/KsJ genome suppressed cellular glucose uptake rates, pancreatic tissue wts. and insulin concns. in both db/db and ob/ob mutants relative to /6 background strain influences or +/ indexes. Concurrent enhancement of tissue and cellular lipogenic metabolism and islet cytolipid depositions were exaggerated when the mutations were expressed on the -/KsJ background relative to the -/6 genome. Pancreatic islet B-cell lipodeposition was markedly enhanced in ob/ob and db/db mutants expressed on either the -/KsJ or -/6 background. In both ob/ob and db/dbmodels, B-cell insulin granulation was prominent in mildly hypertrophic pancreatic islets when the mutations were expressed on the -/6 background. In contrast, the severity of the DOS state expressed on the -/KsJ background resulted in pronounced B-cell atrophy, characterized by insulin degranulation, cellular hypertrophy and hypercytolipidemia associated with tissue involution, in both ob/ob and db/db mutants. Dramatic alterations in tissue **norephinephrine** (NE) and alpha-1-receptor populations in ob/ob and db/db mutants were exaggerated by the -/KsJ genome as compared to -/6 or control indexes. The influences of the -/KsJ genome on the progressive expression of tissue NE counter-regulatory responses to enhanced cytolipidemic indexes were inversely related, with cytochem. lipodeposition occurring under conditions of diminished adrenergic responses to the DOS indexes. The results of these studies indicate that the severity of the type-II diabetes endometabolic syndrome induced by the ob/ob or db/db genotypic mutations is modified by the existing genome on which the mutations are expressed. These data suggest that the severity of genomic mutation expression may by modified depending on the capability of the background genome to counter-regulate the systemic, cellular or metabolic consequences of these mutations.

ACCESSION NUMBER: 2004:805329 CAPLUS
TITLE: Cytochemical Analysis of Pancreatic Islet Hypercytolipidemia following Diabetes (db/db) and Obese (ob/ob) Mutation Expression: Influence of Genomic Background
AUTHOR(S): Garris, David R.; Garris, Bryan L.
CORPORATE SOURCE: Division of Cell Biology and Biophysics, Schools of Biological Sciences and Medicine, University of Missouri-Kansas City, Kansas City, MO, USA
SOURCE: Pathobiology (2004), 71(5), 231-240

L16 ANSWER 3 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CODEN: PATHEF; ISSN: 1015-2008
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Cognitive dysfunction can be treated by administering to a mammal an effective amount of a compound that is an N-methyl-D-aspartate (NMDA) receptor antagonist and a selective norepinephrine (NE) serotonin (5-HT) reuptake inhibitor (NSRI), most preferably between 1:1 and 20:1 NE:5-HT reuptake. In a preferred embodiment the composition includes a pharmaceutically acceptable carrier and an effective cognition-enhancing amount of milnacipran, most preferably about 25 mg/day to about 250 mg/day. The composition may further include at least one of Ginkgo biloba, huperzine A, phosphatidylserine, vitamin E, tacrine, donepezil, rivastigmine, and galantamine. The composition can also include at least one of sibutramine, an aminocyclopropane derivative, venlafaxine, duloxetine, desipramine, nortriptyline, protriptyline, amitriptyline, clomipramine, doxepine, imipramine, and trimipramine.

ACCESSION NUMBER: 2004:453075 CAPLUS
DOCUMENT NUMBER: 140:417969
TITLE: NMDA receptor antagonist-**norepinephrine**-serotonin reuptake inhibitor for the treatment of cognitive dysfunction, and use with other agents
INVENTOR(S): Rao, Srinivas G.; Kranzler, Jay D.
PATENT ASSIGNEE(S): Cypress Bioscience, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045718	A2	20040603	WO 2003-US36813	20031118
WO 2004045718	A3	20040812		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:
US 2002-427767P P 20021120
US 2003-443142P P 20030128
US 2003-479761P P 20030618

OTHER SOURCE(S): MARPAT 140:417969

L16 ANSWER 5 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

BR 2000015320	A	20020709	BR 2000-15320	20001103
EP 1246806	A1	20021009	EP 2000-976885	20001103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR				
JP 2003513074	T2	20030408	JP 2001-534777	20001103
US 2002143014	A1	20021003	US 2002-91949	20020306
US 6579885	B2	20030617		
US 2003203920	A1	20031030	US 2003-426097	20030429

PRIORITY APPLN. INFO.:
US 1999-163269P P 19991103
US 2000-704305 B1 20001102
WO 2000-US30329 W 20001103
US 2002-91949 A3 20020306

OTHER SOURCE(S): MARPAT 134:353258
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
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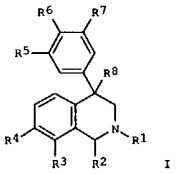

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AB Diarylmethyltetrahydroisoquinolines (4R)- or (4S)-I [R1 = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl; R2 = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, haloalkyl; R3 = H, halogen, (un)substituted OH, S(O)nH, CN, CHO, CONH2, alkyl, alkenyl, alkynyl, cycloalkyl; R4 = (un)substituted aryl, heteroaryl; R5-R7 = H, halogen, CN, (un)substituted OH, NH2, S(O)nH, CHO, CONH2, alkyl, alkenyl, alkynyl, cycloalkyl; R8 = H, (un)substituted OH; n = 0-2] were prepared for use as blockers of the reuptake of norepinephrine, dopamine and serotonin (no data). Thus, 3-bromobenzaldehyde is stirred in the presence of methylamine and reduced with sodium borohydride followed by addition of α-chloroacetophenone and reduction of the amino ketone in situ with sodium borohydride to give 3-BrC6H4CH2N(Me)CH2CH(OH)Ph; cyclization of the benzyl alc. with sulfuric acid followed by coupling with phenylboronic acid gave I (R1 = Me; R4 = Ph; R2 = R3 = R5 = R6 = R7 = H) as an oil. Such compds. are particularly useful in the treatment of a neurol. and psychiatric disorders which are created by or are dependent upon decreased availability of serotonin, norepinephrine or dopamine, such as attention deficit-hyperactivity disorder (ADHD), anxiety, depression, and addiction disorders.

ACCESSION NUMBER: 2001:338496 CAPLUS
DOCUMENT NUMBER: 134:353258
TITLE: Aryl- and heteroaryl-substituted tetrahydroisoquinolines and use thereof to block reuptake of norepinephrine, dopamine and serotonin
INVENTOR(S): Beck, James P.; Curry, Matt A.; Smith, Mark A.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032625	A1	20010510	WO 2000-US30329	20001103
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2389306	AA	20010510	CA 2000-2389306	20001103

L16 ANSWER 6 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Background. Increased availability of norepinephrine (NE) for activation of cardiac adrenoceptors (increased cardiac adrenergic drive) and depletion of myocardial NE stores may contribute to the pathophysiol. and progression of congestive heart failure. This study used a comprehensive neurochem. approach to examine the mechanisms responsible for these abnormalities. Methods and Results. Subjects with and without congestive heart failure received i.v. infusions of [3H]NE. Cardiac spillover, reuptake, vesicular-axoplasmic exchange, and tissue stores of NE were assessed from arterial and coronary venous plasma concns. of endogenous and [3H]-labeled NE and dihydroxyphenylglycol. Tyrosine hydroxylase activity was assessed from plasma dopa, and NE turnover was assessed from measurements of NE metabolites. NE release and reuptake were both increased in the failing heart; however, the efficiency of NE reuptake was reduced such that cardiac spillover of NE was increased disproportionately more than neuronal release of NE. Cardiac NE stores were 47% lower and the rate of vesicular leakage of NE was 42% lower in the failing than in the normal heart. Cardiac spillover of dopa and NE turnover were increased similarly in congestive heart failure. Conclusions. Increased neuronal release of NE and decreased efficiency of NE reuptake both contribute to increased cardiac adrenergic drive in congestive heart failure. Decreased vesicular leakage of NE, secondary to decreased myocardial stores of NE, limits the increase in cardiac NE turnover in CHF. Decreased NE store size in the failing heart appears to result not from insufficient tyrosine hydroxylation but from chronically increased NE turnover and reduced efficiency of NE reuptake and storage.

ACCESSION NUMBER: 1996:307880 CAPLUS
DOCUMENT NUMBER: 125:7188
TITLE: Cardiac sympathetic nerve function in congestive heart failure
AUTHOR(S): Eisenhofer, Graeme; Friberg, Peter; Rundqvist, Bengt; Quyyumi, Arshed A.; Lambert, Gavin; Kaye, David M.; Kopin, Irwin J.; Goldstein, David S.; Esler, Murray D.
CORPORATE SOURCE: National Institute Neurological Disorders and Stroke, National Institutes Health, Bethesda, MD, 20892-1424, USA
SOURCE: Circulation (1996), 93(9), 1667-1676
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 7 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB The authors summarized behavioral and immunocytochem. results from rats with exptl. parkinsonism which were implanted with dopamine- or norepinephrine-containing microspheres. Implanted microspheres containing dopamine and **norephinephrine** attenuated apomorphine-induced rotational behavior in rats with chronic unilateral 6-hydroxydopamine lesions of the ascending (nigrostriatal) dopaminergic neurons. The catecholamine-containing microspheres also stimulated fiber growth in the striatum and fiber growth was related to functional recovery.

ACCESSION NUMBER: 1995:952644 CAPLUS
DOCUMENT NUMBER: 124:1284
TITLE: Catecholamine-containing biodegradable microsphere implants: An overview of experimental studies in dopamine-lesioned rats
AUTHOR(S): McRae, Amanda; Dahlstroem, Annica; Hjorth, Stephan; Ling, Eng Ang; Mason, David; Tice, Thomas
CORPORATE SOURCE: Department Anatomy, University Goteborg, Goeteborg, Swed.
SOURCE: Advances in Behavioral Biology (1995), 44(Alzheimers and Parkinsons Diseases), 421-7
CODEN: ADBBBW; ISSN: 0099-6246
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 8 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB A method was developed for detection of bromodeoxyuridine (BrdU) in conjunction with other antigens in formalin-fixed paraffin sections with microwave antigen retrieval. The method was applied to rat adrenal medulla to demonstrate S-phase nuclei in epinephrine-producing cells strained for immunoreactive phenylethanolamine-N-methyltransferase and in **norephinephrine**-producing cells stained for immunoreactive tyrosine hydroxylase. The quality for staining for all three antigens was comparable to or better than that previously obtained with other techniques. This method provides an efficient tool for studying turnover of subpopulations of adrenal chromaffin cells. It should also be widely applicable to other cells and tissues.

ACCESSION NUMBER: 1995:316663 CAPLUS
DOCUMENT NUMBER: 122:155579
TITLE: Triple immunohistochemical staining for bromodeoxyuridine and catecholamine biosynthetic enzymes using microwave antigen retrieval
AUTHOR(S): Tischler, Arthur S.
CORPORATE SOURCE: Department of Pathology, Tufts University School of Medicine, Boston, MA, USA
SOURCE: Journal of Histochemistry and Cytochemistry (1995), 43(1), 1-4
CODEN: JHCYAS; ISSN: 0022-1554
PUBLISHER: Histochemical Society, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 9 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB We have previously found that histamine H3-receptors are neg. coupled to norepinephrine exocytosis in atrial tissue. We report here that in the presence of H1- and H2-receptor blockers, histamine significantly inhibits the tachycardia and norepinephrine release elicited by sympathetic nerve stimulation in isolated guinea pig hearts, an effect prevented by the H3 antagonist, thiperamide. Sympathetic nerve stimulation also caused a 1.5-fold increase in histamine overflow, which was insufficient to activate H3 receptors because thioperamide affected neither the tachycardia nor the norepinephrine release. Hence, we questioned whether H3 receptors become activated when adrenergic activity is greatly enhanced, as in myocardial ischemia. Guinea pig hearts underwent 10-min global ischemia. At reperfusion, norepinephrine exocytosis was markedly augmented and was associated with a 3.5-fold increase in histamine overflow. (R)α-methylhistamine, an H3 agonist, did not modify **norephinephrine** release, whereas thioperamide doubled it. Thus, in physiol. conditions, cardiac H3 receptors are quiescent, yet available for activation by exogenous ligands. In contrast, in the ischemic myocardium, H3 receptors appear to be fully activated by an endogenous ligand, probably histamine. Hence, cardiac H3 receptors may play an important role by neg. modulating exocytotic **norephinephrine** release associated with ischemic states.

ACCESSION NUMBER: 1995:273654 CAPLUS
DOCUMENT NUMBER: 122:78176
TITLE: Unmasking of activated histamine H3-receptors in myocardial ischemia: their role as regulators of exocytotic norepinephrine release
AUTHOR(S): Imamura, Michiaki; Poli, Enzo; Omoniyi, Abimbola T.; Levi, Roberto
CORPORATE SOURCE: Department of Pharmacology, Cornell University Medical College, New York, NY, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1994), 271(3), 1259-66
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 10 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB The authors hypothesized, first, that recent antecedent hypoglycemia causes reduced autonomic responses to subsequent hypoglycemia in patients with well-controlled insulin-dependent diabetes mellitus (IDDM) and that the reduced responses are specific for the stimulus of hypoglycemia while the responses to other stimuli are unaltered and, second, that reduced autonomic responses, specifically sympathochromaffin, so-induced are not simply the result of prior activation of the system. To test the first hypothesis, eight patients with IDDM, selected for HbAlc levels <8.0% and the absence of classic diabetic autonomic neuropathy, were studied twice. On one occasion, clamped hypoglycemia (.apprx.2.8 mM) was produced at 1400-1600 on days 2 and 3; on the other occasion clamped euglycemia (.apprx.5.6 mM) was produced at those times. On both occasions, autonomic responses to hypoglycemia (.apprx.2.8 mM) were determined the morning of day 3 and those to standing, exercise, and a formula meal the morning of day 4. Following afternoon hypoglycemia, 1) the adrenomedullary epinephrine (EPI) response to hypoglycemia was reduced (P = 0.0397) but that to standing, exercise, and a meal were unaltered; 2) the sympathetic neural **norephinephrine** (NE) response to standing and to exercise was unaltered; and 3) the partially parasympathetic neural-mediated pancreatic polypeptide response to a meal was unaltered.

ACCESSION NUMBER: 1994:505793 CAPLUS
DOCUMENT NUMBER: 121:105793
TITLE: Hypoglycemia-induced autonomic failure in IDDM is specific for stimulus of hypoglycemia and is not attributable to prior autonomic activation
AUTHOR(S): Rattarasarn, Chatchalit; Dagogo-Jack, Samuel; Zachwieja, Jeffery J.; Cryer, Philip E.
CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, USA
SOURCE: Diabetes (1994), 43(6), 809-18
CODEN: DIAEAZ; ISSN: 0012-1797
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 11 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB The influence of a 1.75 g dose of ascorbic acid on subsequent 4-h urinary excretion of Ca and free dopamine, norepinephrine, and epinephrine was investigated in 38 young women. Small increases, relative to control values from the same subjects, were observed for both urinary Ca and urinary dopamine. No significant changes were observed in urinary **norephinephrine**, epinephrine, P, creatinine, volume, or pH. Stepwise multiple regression anal. was used to evaluate factors as predictors for the Ca in the control urine sample, the Ca in the urine sample following the ascorbic acid dose, and for the difference in Ca excretion in the 2 situations. In the equation predicting the difference in urinary Ca, difference in urinary dopamine was a highly significant factor, μg dopamine explaining 29% of the variance in mg Ca. Dopamine was also a significant factor in the equation for predicting Ca excretion in the ascorbic acid dose situation but was not significant in the control situation. These findings indicate some apparent effects of acute ascorbic acid administration and raise the question whether endogenous dopamine is involved in some aspect of Ca homeostasis.

ACCESSION NUMBER: 1993:58581 CAPLUS
DOCUMENT NUMBER: 118:58581
TITLE: Urinary excretion of calcium, dopamine, norepinephrine, and epinephrine in young women following ascorbic acid ingestion
AUTHOR(S): Long, Karen P.; Marcuson, Richard; Miyashita, Koichi; Tsao, Constance S.
CORPORATE SOURCE: Dep. Chem., Diablo Valley Coll., Pleasant Hill, CA, 94523, USA
SOURCE: Nutrition Research (New York, NY, United States) (1992), 12(9), 1051-63
CODEN: NTRSDC; ISSN: 0271-5317
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 12 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Epinephrine-producing cells are characterized by the presence of phenylethanolamine N-methyltransferase (PNMT), which catalyzes the formation of epinephrine from norepinephrine. A line of transgenic mice was generated which carry a chimeric gene containing human PNMT cDNA fused to the 4-kilobase fragment of the human dopamine β-hydroxylase (DBH) gene promoter, to switch catecholamine phenotype in the nervous and endocrine systems. Human PNMT transcripts and immunoreactivity were mainly detected in norepinephrine neurons in brain and sympathetic ganglion as well as in norepinephrine-producing cells in adrenal medulla of transgenic mice, indicating that the human DBH gene promoter of 4 kilobases is sufficient to direct expression of the gene in norepinephrine-producing cells. Anal. of catecholamines in the various tissues showed that the expression of human PNMT in transgenic mice induced the appearance of epinephrine in sympathetic ganglion and dramatic changes in norepinephrine and epinephrine levels in brain, adrenal gland, and blood. These results indicate that the addnl. PNMT expression in norepinephrine-producing cells can convert these cells to the epinephrine phenotype, and suggest that norepinephrine-producing cells normally possess the basic machinery required for the synthesis of epinephrine except for PNMT. Thus it appears that the only major difference between norepinephrine- and epinephrine-producing cells is the expression of PNMT. The transgenic animals provide an exptl. model to investigate the functional differences between norepinephrine and epinephrine.

ACCESSION NUMBER: 1992:228758 CAPLUS
DOCUMENT NUMBER: 116:228758
TITLE: Genetic alteration of catecholamine specificity in transgenic mice
AUTHOR(S): Kobayashi, Kazuto; Sasaoka, Toshikuni; Morita, Shinji; Nagatsu, Ikuko; Iguchi, Akihisa; Kurosawa, Yoshikazu; Fujita, Keisuke; Nomura, Tatsuji; Kimura, Minoru; et al.
CORPORATE SOURCE: Sch. Med., Fujita Health Univ., Toyoake, 470-11, Japan
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1992), 89(5), 1631-5
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 13 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Rat brain cortex synaptosomes pre-incubated with [3H] **norephinephrine** were used (1) to provide evidence that part of the NMDA receptors mediating stimulation of norepinephrine (NE) release are located on the noradrenergic varicosities themselves, (2) to characterize these receptors and (3) to examine whether ethanol specifically inhibits the NMDA-evoked NE release via a presynaptic site of action. In synaptosomes superfused with Mg2+-free Krebs-Henseleit solution, NMDA (2-min exposure) stimulated tritium overflow in a concentration- and glycine-dependent manner. The stimulatory effect of NMDA was not altered by tetrodotoxin but was abolished by omission of Ca2+ from the superfusion fluid and was considerably reduced in the presence of 1.2 mM Mg2+. DL-(E)-2-Amino-4-methyl-5-phosphono-3-pentanoic acid (CGP 37849; a competitive NMDA receptor antagonist) produced a parallel shift of the concentration-response curve for NMDA to the right, whereas dizocilpine (MK-801; an antagonist at the phencyclidine, PCP, recognition site of the NMDA-gated ion channel) reduced the maximum effect of NMDA. Ethanol inhibited the NMDA-evoked tritium overflow in a concentration-dependent manner. In contrast, in synaptosomes superfused with Ca2+-free Krebs-Henseleit solution containing 15 mM K+ throughout, ethanol did not affect the tritium overflow evoked by 2 min introduction of 75 μM Ca2+ into the superfusion fluid. This Ca2+-evoked overflow was also not altered by tetrodotoxin and dizocilpine, but was inhibited by the inorg. Ca2+ channel antagonist Cd2+. Therefore, (1) NMDA receptors mediating stimulation of NE release are also located on the cortical noradrenergic varicosities (and not only on so far unknown excitatory interneurones within the cortex); (2) these receptors exhibit the characteristic pharmacol. features of the NMDA receptor system; (3) ethanol selectively inhibits the NE release evoked by stimulation of the presynaptic NMDA receptors, leaving the Ca2+-evoked release promoted by high K+ unaffected. This finding is compatible with the suggestions that the NMDA receptor system itself is a site of action of ethanol.

ACCESSION NUMBER: 1992:168219 CAPLUS
DOCUMENT NUMBER: 116:168219
TITLE: Presynaptic site of action underlying the ethanol-induced inhibition of norepinephrine release evoked by stimulation of N-methyl-D-aspartate (NMDA) receptors in rat cerebral cortex
AUTHOR(S): Fink, Klaus; Goethert, Manfred
CORPORATE SOURCE: Inst. Pharmacol. Toxicol., Univ. Bonn, Bonn, D-5300, Germany
SOURCE: Brain Research (1992), 572(1-2), 27-32
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 14 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB **Effects of norephinephrine** (NE, 10-6 M), epinephrine (E, 10-6 M), and vehicle on coronary blood flow (CF), oxygen consumption, and lactate release were compared in 32 isolated rat hearts during 5 min of ventricular fibrillation (VF). After VF, tissue concns. of ATP, AMP, creatinine phosphate (CP), and lactate were measured. Perfusion of treatments started 30 s after onset of VF and was maintained throughout VF. CF during VF was greater during perfusion of E (5.73 mL/min) than NE (5.06 mL/min) or vehicle (5.11 mL/min). Oxygen consumption during VF was higher during perfusion of E (29.5 μL·min-1·g wet heart wt-1) than vehicle (27.3 μL·min-1·g-1); average oxygen consumption during NE (27.6 μL·min-1·g-1) and vehicle were comparable. After NE, but not E, tissue AMP concns. were increased, and CP concns. were reduced compared with vehicle. Enhanced consumption of high-energy phosphates during NE suggests that there is also an enhanced demand for oxygen. However, unlike during E, during NE this demand is not met by an augmented CF. Thus, compared with E, NE treatment during VF may increase the risk of hypoxic damage.

ACCESSION NUMBER: 1992:19115 CAPLUS
DOCUMENT NUMBER: 116:19115
TITLE: Adrenergic influences on cardiac function during ventricular fibrillation in isolated rat hearts
AUTHOR(S): Derad, I.; Funk, I.; Pauschinger, P.; Born, J.
CORPORATE SOURCE: Univ. Ulm, Ulm, 7900, Germany
SOURCE: American Journal of Physiology (1991), 261(5, Pt. 2), H1452-6
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 15 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB This study was carried out to investigate the possibility of local epinephrine (E) synthesis in rat cardiac tissue and to study the effect of bilateral adrenalectomy (A DX) on catecholamine synthesis. Bilateral adrenalectomy reduced cardiac and plasma E levels, but a substantial amount of E (33.3%) was retained in the atrium 9 days after bilateral adrenalectomy. There were also redns. in atrial **norephinephrine** (NE) and dopamine (DA) as well as ventricular DA. Cardiac E-forming activity (EFA) was not affected in ADX rats, but ventricular EFA showed a 42.3% increase compared to sham operated (SH) rats. Cardiac dopamine β-hydroxylase (DBH) activity was increased in the atrium (31%) and in the ventricle (60%) of ADX rats compared to SH rats. In SH rats, decapitation increased plasma E 61-fold but lowered plasma DA levels compared to the corresponding rest values, indicating that plasma DA is incorporated in the synthesis of catecholamines in the adrenal medulla. Thus, cardiac tissue synthesizes its own E and bilateral adrenalectomy increases sympathetic activity, catecholamine synthesis, and NE turnover.

ACCESSION NUMBER: 1991:624423 CAPLUS
DOCUMENT NUMBER: 115:224423
TITLE: Effect of bilateral adrenalectomy on catecholamine synthesis in the rat heart
AUTHOR(S): Elayan, Hamzeh H.; Gharaibeh, Munir N.
CORPORATE SOURCE: Fac. Med., Univ. Leeds, UK
SOURCE: Dirasat - University of Jordan (1989), 16(4), 115-29
CODEN: DUJOES; ISSN: 0255-8033
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 16 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB This study investigated the effects of iontophoretic application of excitatory amino acid (EAA) and norepinephrine (NE) agonists and antagonists on synaptic transmission to individual jaw-opener motoneurons (digastric) during activation of the jaw-opening reflex (JOR) evoked by stimulation of either fibers within the oral mucosa (OM) or tooth-pulp (TP). During both OM and TP stimulation, kynurenic acid (KYN), a wide-spectrum EAA antagonist, suppressed jaw-opener motoneuron discharge. Application of DL-2-amino-5-phosphonovaleric acid (APV), an NMDA receptor antagonist, also suppressed motoneuron discharge evoked by TP stimulation, but produced minimal effects on motoneuron discharge evoked by OM stimulation. These data suggest a role of EAA in mediating synaptic transmission from last-order interneurons to jaw-opener motoneurons during the jaw-opening reflex evoked by intra-oral stimulation. Iontophoretic application of NE produced dual effects (facilitation or suppression) on motoneuronal discharge evoked by OM or TP stimulation. The effects were not related to the mode of motoneuronal activation. Iontophoretic application of the α1 agonist, phenylephrine, facilitated motoneuronal discharge. In contrast, application of the α2 agonist, clonidine, suppressed motoneuronal discharge during intra-oral stimulation. These effects were antagonized by prior iontophoretic application of the α1 antagonist, prazosin, or the α2 antagonist, yohimbine, resp. In those cells in which the predominant effect of NE application on synaptic transmission was either facilitation or suppression of motoneuronal discharge, prior iontophoretic application of prazosin or yohimbine, resp., antagonized the effects of NE application. These data suggest that NE can modulate synaptic transmission to jaw-opener motoneurons evoked by intra-oral stimulation via activation of α1 or α2 adrenoreceptors on trigeminal motoneurons.

ACCESSION NUMBER: 1991:528119 CAPLUS
DOCUMENT NUMBER: 115:128119
TITLE: Iontophoretic analysis of the pharmacologic mechanisms responsible for initiation and modulation of trigeminal motoneuronal discharge evoked by intra-oral afferent stimulation
AUTHOR(S): Katakura, Nobuo; Chandler, Scott H.
CORPORATE SOURCE: Brain Res. Inst., Univ. California, Los Angeles, CA, 90024, USA
SOURCE: Brain Research (1991), 549(1), 66-77
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 17 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB To define the role of noradrenergic regulation of growth hormone (GH) secretion in a primate species, spontaneous and GH-releasing hormone (GHRH) stimulated GH secretion was studied in 6 chronically catheterized adult male cynomolgus monkeys before and after inhibition of norepinephrine synthesis. Blood samples were obtained at 15-min intervals over 8 h to characterize the pattern of GH secretion, and the GH response to GHRH (10 μg/kg, i.v.) was determined These measurements were repeated 2 wk later, 2 h after the i.v. administration of 12.5 mg/kg of the dopamine β-hydroxylase inhibitor diethyldithiocarbamate (DDTC), which has been shown to be effective norepinephrine synthesis inhibitor in the rat. Spontaneous and stimulated GH secretory patterns before and after DDTC administration were compared. Both the frequency and the amplitude of spontaneous GH pulses were markedly reduced by DDTC (3.8 before vs. 1.8 peaks/8 h after DDTC and 5.5 vs 2.0 ng/mL). Areas under the curve were also reduced by DDTC treatment (10.8 vs. 5.7 ng + h/mL), and DDTC administration diminished the peak GH responses to GHRH(12 vs. 4 ng/mL). These results are consistent with the belief that DDTC is a potent inhibitor of spontaneous and GHRH-induced GH secretion. The action of DDTC could be mediated by a reduction in GHRH due to reduced norepinephrine synthesis, by an increase in somatostatin release through a dopaminergic stimulus, or by a direct dopaminergic effect on somatotrophs.

ACCESSION NUMBER: 1990:112436 CAPLUS
DOCUMENT NUMBER: 112:112436
TITLE: Effects of inhibition of norepinephrine synthesis on spontaneous and growth hormone-releasing hormone-induced GH secretion in cynomolgus macaques: evidence for increased hypothalamic somatostatin tone
AUTHOR(S): Malozowski, Saul; Hao, En Hui; Ren, Song Guang; Genazzani, Alessandro D.; Kalogeras, Konstatine T.; Merriam, George R.
CORPORATE SOURCE: Dev. Endocrinol. Branch, Natl. Inst. Child Health and Hum. Dev., Bethesda, MD, 20892, USA
SOURCE: Neuroendocrinology (1990), 51(4), 455-8
CODEN: NUNDAJ; ISSN: 0028-3835
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 18 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB To investigate the possible involvement of pp60c-src in exocytosis, cultured bovine chromaffin cells were analyzed for changes in c-src tyrosine kinase activity in response to stimulation by several secretagogues. Results of in vitro immune complex kinase assays showed that pp60c-src, derived from cells that had been stimulated for various lengths of time, exhibited decreased auto- and transphosphorylating activities as compared to pp60c-src immunopptd. from control cells. The greatest reduction in activity was observed 10 min post-stimulation, whereas normal levels were regained 2-6 g after secretagogue treatment. Western immunoblot anal. of the immunopptd. pp60c-src revealed that .apprx.50% less c-src protein was present in immune complexes prepared 10 min after stimulation as compared to those prepared from mock-stimulated controls, resulting in a specific autophosphorylating activity that was 42-47% of control and little or no reduction in the transphosphorylating specific activity. In expts. in which the rate of secretion of [3H]norepinephrine from cells preloaded with this compound was compared to the rate of modulation of pp60c-src activity, 50% of the maximal reduction in pp60c-src activity occurred within 2-4 min, whereas 50% maximal release of [3H] **norephinephrine** occurred within 1-3 min. Apparently, pp60c-src may play some role (direct or indirect) in the exocytotic process.

ACCESSION NUMBER: 1989:612420 CAPLUS
DOCUMENT NUMBER: 111:212420
TITLE: Modulation of pp60c-src tyrosine kinase activity during secretion in stimulated bovine adrenal chromaffin cells
AUTHOR(S): Oddie, K. M.; Litz, J. S.; Balserak, J. C.; Payne, D. M.; Creutz, C. E.; Parsons, Sarah J.
CORPORATE SOURCE: Sch. Med., Univ. Virginia, Charlottesville, VA, 29908, USA
SOURCE: Journal of Neuroscience Research (1989), 24(1), 38-48
CODEN: JNREDK; ISSN: 0360-4012
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 19 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Repetitive peer sepns. of rhesus monkeys was used to study oxaprotiline effects on various components of the depressive syndrome. This paradigm is sensitive to norepinephrine. Oxaprotiline, a norepinephrine uptake inhibitor, showed results in less severe behavioral reactions to social separation CGP12103A, the (-)isomer of oxaprotiline, which has no effect on **norephinephrine**, should have no effect on the paradigm. However, both isomers caused alterations in certain components of the behavioral response to separation (stereotypy, huddling, locomotion, self-directed behavior and inactivity) and specifically caused a reduction in stereotypic behaviors.

ACCESSION NUMBER: 1989:185800 CAPLUS
DOCUMENT NUMBER: 110:185800
TITLE: Effects of oxaprotiline on the response to peer separation in rhesus monkeys
AUTHOR(S): McKinney, William T.; Kraemer, Gary W.
CORPORATE SOURCE: Sch. Med., Univ. Wisconsin, Madison, WI, USA
SOURCE: Biological Psychiatry (1989), 25(6), 818-21
CODEN: BIPCBP; ISSN: 0006-3223
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 20 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Differential effects of 2 calmodulin antagonists, W-7 and W-5, on synapsin I phosphorylation and norepinephrine release associated with Ca2+ influx, were investigated using [32P]phosphate in synaptosomes derived from rat cerebral cortex. The Ca2+ ionophore (A23187)-stimulatory effect on synapsin I phosphorylation and norepinephrine release was markedly reduced by W-7 and slightly reduced by W-5, whereas neither the strong nor the weak calmodulin antagonist had an effect on A23187-stimulated synaptosomal uptake of Ca2+. Preincubation with H-8 reduced both W-5- and W-7-inhibited A23187-stimulated synapsin I phosphorylation by the same amount but did not affect their inhibitory effect nor the ionophore-stimulated norepinephrine release, thereby suggesting that W-5 may serve as an appropriate control for the noncalmodulin-mediated effect of both calmodulin antagonists.

ACCESSION NUMBER: 1989:53099 CAPLUS
DOCUMENT NUMBER: 110:53099
TITLE: Clearer demonstration of calcium/calmodulin-dependent events in synaptosomes by use of the differential effects of two calmodulin antagonists, N-(aminohexyl)-5-chloro-1-naphthalenesulfonamide and N-(6-aminohexyl)-1-naphthalenesulfonamide
AUTHOR(S): Imai, Shizuko; Onozuka, Minoru
CORPORATE SOURCE: Sch. Med., Gifu Univ., Gifu, 500, Japan
SOURCE: Comparative Biochemistry and Physiology, Part C: Pharmacology, Toxicology & Endocrinology (1988), 91C(2), 535-40
CODEN: CBPCEE; ISSN: 0742-8413
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 21 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Nerve degeneration techniques (ganglionectomy, interganglionic secretion, postganglionic axotomy, uni- or bilateral hypogastric nerve section, and right pelvic ganglionectomy) and fluorometric detns. of histamine and **norephinephrine** showed the presence of nervous pathways containing histamine adjacent to the sympathetic system of the rat vas deferens. Apparently, these pathways cross between the ganglionic clusters located at the angle formed by the seminal vesicle and the vas deferens. They are not structurally related to the central nervous system by way of the hypogastric or pelvic ganglion. The histamine-containing pathways were independent of the noradrenergic pathways, as dissociation between norepinephrine depletion and histamine depletion was shown under nerve degeneration. The time course of nerve degeneration over a long period after sympathectomy showed a biphasic effect on histamine levels of the vas deferens. The early histamine depletion was indicative of degeneration of histamine-containing pathways, and the delayed histamine increasing phase was considered to be due to the accumulation of mast cells in the degenerating nerve sheaths. A possible role for the histamine-containing pathways in the modulation of sympathetic activity is envisaged.

ACCESSION NUMBER: 1988:180681 CAPLUS
DOCUMENT NUMBER: 108:180681
TITLE: A possible crossed histamine-containing pathway adjacent to the sympathetic system of the rat vas deferens
AUTHOR(S): Campos, H. Augusto
CORPORATE SOURCE: Vargas Med. Sch., Cent. Univ. Venezuela, Caracas, 1070-A, Venez.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1988), 244(3), 1121-7
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 22 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB The effect of dihydroxyphenylacetic acid (DOPAC), the 1st deaminated metabolite of dopamine (DA), on norepinephrine (NE) accumulation in the brain after s.c. L-dopa treatment was studied in rats. Intracerebroventricular injection of DOPAC before or after L-dopa treatment had no effect on DA and NE concns. in the rat brain. In rats pretreated with pargyline, a DA deamination inhibitor, and injected with L-dopa, high concns. of DOPAC did not restrict NE accumulation.

ACCESSION NUMBER: 1988:179968 CAPLUS
DOCUMENT NUMBER: 108:179968
TITLE: Effect of intraventricular injections of 3,4-dihydroxyphenylacetic acid (DOPAC) on cerebral norepinephrine accumulation in L-dopa treated rats
AUTHOR(S): Boudet, C.; Buu, N. T.; Duhaime, J.; Kuchel, O.; Peyrin, L.
CORPORATE SOURCE: Lab. Physiol., Fac. Med. Grange-Blanche, Lyon, 69373, Fr.
SOURCE: Biogenic Amines (1987), 4(4-6), 413-17
CODEN: BIAME7; ISSN: 0168-8561
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 23 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB The vascular responses to acetylcholine (ACh), norepinephrine (NE), KCl, and diltiazem were examined before and after removal of endothelial cells by an intraluminal bolus injection of saponin (1 mg) in isolated and perfused dog coronary arteries. Without any precontraction, ACh induced a long-lasting vasodilation in small doses (<1 μg), and an initial brief vasoconstriction was occasionally accompanied in large doses. These vascular responses to ACh were not significantly affected by the pretreatment with propranolol (5 + 10-6 mol/L). The endothelial removal by intraluminal saponin was confirmed electron microscopically. After 20-60 min of saponin treatment, the ACh-induced vasodilation was significantly attenuated by saponin, but the ACh-induced vasoconstriction was not affected by it. The vasodilation was blocked by atropine. The NE- and KCl-induced vasoconstrictions and diltiazem-induced vasodilation were not affected by saponin treatment. Thus ACh produced a vasodilation in the nonpreconstricted condition of dog coronary arteries, the vasodilation caused by ACh is mostly endothelium-dependent and considered to be mediated by muscarinic receptors, and the vascular responses to NE, KCl, and diltiazem and the vasoconstriction produced by ACh are not influenced by removal of the endothelium in a relatively large epicardial coronary artery of the dog.

ACCESSION NUMBER: 1987:452624 CAPLUS
DOCUMENT NUMBER: 107:52624
TITLE: Responses of isolated and perfused dog coronary arteries to acetylcholine, norepinephrine, potassium chloride, and diltiazem before and after removal of the endothelial cells by saponin
AUTHOR(S): Nakane, Tokio; Ito, Nobuo; Chiba, Shigetoshi
CORPORATE SOURCE: Sch. Med., Shinshu Univ., Matsumoto, 390, Japan
SOURCE: Heart and Vessels (1986), 2(4), 221-7
CODEN: HEVEEO; ISSN: 0910-8327
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 24 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB The recovery of plasma glucose and the responses of counterregulatory hormone after insulin-induced hypoglycemia were investigated in 7 normal controls and 16 non-insulin-dependent diabetic patients (NIDDM). Seven of the diabetics (group A) had no autonomic neuropathy, and 9 (group B) had autonomic neuropathy. There were no differences in the rate of plasma glucose decrement and the nadir glucose concentration in the 3 groups. The incremental areas of plasma glucose concentration from 15 (glucose nadir) to 90 min were 2267, 2132, and 874 mg/min/dL in controls and groups A and B, resp. The increment in group B was lower than in the other groups. The incremental areas of each hormone from 0 to 90 min after the end of insulin infusion were calculated ΣΔ Glucagon (IRG) in controls and groups A and B was 2210, 2369, and 762 pg/min/mL, resp. The EAIRG in group B was lower than that in group A. ΣΔ Epinephrine (PE) was 4.95 ng/min/mL in controls, 6.89 in group A, and 3.04 in group B. ΣΔPE in group B was lower compared with that in group A. ΣΔ **Norephinephrine** (PNE) in controls and groups A and B was, 3.36, 4.05, and 1.83 ng/min/mL, resp. ΣΔPNE in group B was lower than in the others. There were no differences in ΣΔ growth hormone and ΣΔ cortisol in the 3 groups. The glucose recovery and the increments of counterregulatory hormone were similar in the controls and the NIDDM patients without autonomic neuropathy, whereas the glucose recovery was delayed in the NIDDM patients with autonomic neuropathy due to reduced secretion of glucagon and catecholamines. Heart rate variations in the groups are described. Apparently, autonomic nervous activity is of major importance for counterregulatory hormone secretion after hypoglycemia in NIDDM patients. Whether NIDDM patients, if treated strictly with insulin, have an increased risk for hypoglycemia must be assessed in advance by testing autonomic function.

ACCESSION NUMBER: 1986:107310 CAPLUS
DOCUMENT NUMBER: 104:107310
TITLE: Quantitative evaluation of diabetic autonomic neuropathy based on heart rate variations - Relationship between autonomic neuropathy and counterregulatory hormone secretion after hypoglycemia in non-insulin-dependent diabetic patients
AUTHOR(S): Oikawa, Noboru; Sanoyama, Kyo; Abe, Ryuzo; Sato, Hideyuki; Sakurada, Mikio; Toyota, Takayoshi; Goto, Yoshio
CORPORATE SOURCE: Sch. Med., Tohoku Univ., Sendai, Japan
SOURCE: Tonyobyo (Tokyo, Japan) (1985), 28(9), 1073-9
CODEN: TONYA4; ISSN: 0021-437X
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

L16 ANSWER 25 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

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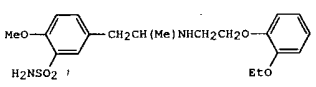

I

AB The effects of YM-12617 (I) [80223-99-0] on the electrophysiol. properties of smooth muscle membranes and prejunctional nerve terminals and contractions evoked by different procedures were studied using guinea pig mesenteric and pulmonary arteries. I (> 1nM) inhibited the depolarization induced by **norephinephrine** in both muscle tissues. Yohimbine had no effect, whereas prazosin inhibited the norepinephrine-induced depolarization to a lesser extent than I. When I (> 1nM) was applied to the mesenteric artery, the amplitude of the 1st excitatory-junction potential evoked by a train stimulation of perivascular nerves was inhibited, but the facilitation of excitatory-junction potentials evoked by frequencies over 0.1 Hz was enhanced. As a consequence, the amplitude of the excitatory junction potentials after completion of the facilitation exceeded the control, as was expected to occur with a typical α2-adrenoceptor blocker. I inhibited the contraction evoked by exogenously applied norepinephrine or perivascular nerve stimulation, with a higher potency than seen with prazosin, but this agent had no effect on the contraction evoked by excess concns. of K+ or by direct muscle stimulation. Apparently, I possesses a more potent α1-adrenoceptor blocking action than does prazosin, and is more selective for α1- than for α2-adrenoceptors.

ACCESSION NUMBER: 1986:102335 CAPLUS
DOCUMENT NUMBER: 104:102335
TITLE: Effects of YM-12617, an alpha adrenoceptor blocking agent, on electrical and mechanical properties of the guinea pig mesenteric and pulmonary arteries
AUTHOR(S): Fujii, Koji; Kuriyama, Hiroshi
CORPORATE SOURCE: Fac. Med., Kyushu Univ., Fukuoka, 812, Japan
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1985), 235(3), 764-70
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 26 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Adrenal secretion rates and arterial plasma epinephrine (E) [51-43-4], **norephinephrine** (NE) [51-41-2], and dopamine [51-61-6] levels were studied in 9 groups of mongrel dogs under pentobarbital anesthesia: (1) resting animals; (2) hemorrhage (25 mL/kg); (3) hemorrhage after acute nephrectomy; (4-7) hemorrhage and acute nephrectomy and i.v. angiotensin II [11128-99-7] at 0.01, 0.10, 1.00, or 10.00 ng/kg/min; (8) no hemorrhage, acute nephrectomy, angiotensin II (10.00 ng/kg/min); and (9) hemorrhage, kidneys intact, i.v. angiotensin II (10.00 ng/kg/min). Arterial and adrenal blood were sampled during a baseline prehemorrhage period and 15, 30, 60, and 90 min after hemorrhage. Results confirmed blunting of reflex E release by acute nephrectomy in the anesthetized dog and showed that angiotensin II restores E, NE, and dopamine release in acutely anephric dogs. Aortic plasma E and NE were also restored to normal by angiotensin II. Dogs with intact kidneys show a blunted hemorrhage response of arterial plasma E, NE, and dopamine to the largest angiotensin II infusion rate (10 ng/kg/min). Apparently, in acutely anephric conditions, angiotensin II support of reflex catecholamine release is sensitively dose dependent to physiol. infusion rates of systemic angiotensin II and this angiotensin II effect is restrained by the kidney.

ACCESSION NUMBER: 1985:607552 CAPLUS
DOCUMENT NUMBER: 103:207552
TITLE: Angiotensin II restoration of reflex adrenal medullary secretion to anephric dogs is physiologically dose dependent
AUTHOR(S): Badder, Elliott M.; Duarte, Bernardo; Seaton, John F.; Hamaji, Masayasu; Harrison, Timothy S.
CORPORATE SOURCE: Med. Sch., Univ. Maryland, Baltimore, MD, 21201, USA
SOURCE: Endocrinology (1985), 117(5), 1920-9
CODEN: ENDOAO; ISSN: 0013-7227
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 27 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB A series of studies were performed to determine the relationship between physiol. levels of circulating plasma norepinephrine [51-41-2] and epinephrine [51-43-4] and human platelet alpha-2 binding site number and the affinity (KD) of these sites for antagonist radioligands. In one study, alpha-2-adrenergic binding site number and affinity were compared using both 3H-labeled yohimbine [146-48-5] and 3H-labeled dihydroergocryptine [25447-66-9] as radioligands. There was good absolute and relative comparison for binding site number, but only a relative relationship for KD. In 46 normal subjects, there was no significant relationship between site number or KD and age, plasma epinephrine, or plasma norepinephrine concentration Even after plasma epinephrine was raised nearly 20-fold by means of an i.v. infusion for 4 h in 7 normal subjects, neither sites (608 vs. 567 sites/platelet) nor KD (2.01 vs. 2.14 nM) were significantly changed. Similarly, neither sites (445 vs. 421 sites/platelet) nor KD (1.44 vs. 2.10 nM) were significantly changed in 6 normal subjects when plasma **norephinephrine** levels increased during oral administration of prazosin for 1 wk. Thus, in a cross-sectional anal. and after a change in plasma catecholamine concns., there was no relationship in normal subjects between platelet alpha-2 binding site number or affinity of these sites for antagonist radioligands and the circulating catecholamine levels to which the platelets were exposed.

ACCESSION NUMBER: 1984:583886 CAPLUS
DOCUMENT NUMBER: 101:183886
TITLE: Variations in circulating catecholamines fail to alter human platelet alpha-2-adrenergic receptor number or affinity for [3H]yohimbine or [3H]dihydroergocryptine
AUTHOR(S): Pfeifer, M. A.; Ward, K.; Malpass, T.; Stratton, J.; Halter, J.; Evans, M.; Beiter, H.; Harker, L. A.; Porte, D., Jr.
CORPORATE SOURCE: Univ. Washington, Seattle, WA, USA
SOURCE: Journal of Clinical Investigation (1984), 74(3), 1063-72
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 28 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Pineal tryptophan [73-22-3], serotonin [50-67-9], serotonin-N-acetyltransferase (NAT) [9027-33-2], melatonin [73-31-4], 5-hydroxyindoleacetic acid [54-16-0], norepinephrine [51-41-2] and dopamine [51-61-6] were measured in castrated rabbits at 11.00, 00.30, and 03.00 h. The rabbits were housed in a light:dark 14:10 (lights on 07.00 h). Significant day:night variations were found in NAT, melatonin, dopamine, and norepinephrine. These results were compared to data on rhythms of pineal constituents in other species.

ACCESSION NUMBER: 1984:564206 CAPLUS
DOCUMENT NUMBER: 101:164206
TITLE: Day:night variations of melatonin, 5-hydroxyindoleacetic acid, serotonin, serotonin N-acetytransferase, tryptophan, **norephinephrine** and dopamine in the rabbit pineal gland
AUTHOR(S): Brainard, George C.; Matthews, Susan A.; Steger, Richard W.; Reiter, Russel J.; Asch, Ricardo H.
CORPORATE SOURCE: Dep. Neurol., Jefferson Med. Coll., Philadelphia, PA, 19107, USA
SOURCE: Life Sciences (1984), 35(15), 1615-22
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 29 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

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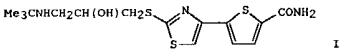

I

AB The effects of arotinolol (I) [68377-92-4] on dog coronary arteries were investigated in vitro. In distal portions of left circumflex coronary arteries contracted with 3 + 10-2 M KCl, **norephinephrine** [51-41-2] relaxed the strips in a concentration-dependent fashion. Propranolol [525-66-6] (10-6 M) converted the norepinephrine-induced relaxations to contractions, and arotinolol (10-6-10-5 M) inhibited the relaxations induced by norepinephrine in a concentration-dependent manner. In proximal portions of the strips after K+ contracture, **norephinephrine** produced concentration-dependent contractions which were augmented by propranolol (10-6 M) and inhibited by arotinolol (10-6-10-5 M). This suggested that arotinolol has an α-adrenoceptor blocking activity in addition to a β-adrenoceptor blocking action in dog coronary arteries.

ACCESSION NUMBER: 1984:503903 CAPLUS
DOCUMENT NUMBER: 101:103903
TITLE: Possible α-adrenoceptor blocking activity of arotinolol (S-596), a new β-adrenoceptor blocking agent in isolated dog coronary artery
AUTHOR(S): Sakanashi, Matao; Miyamoto, Yoshimasa; Ito, Hirosumi; Takeo, Satoshi; Noguchi, Katsuhiko; Higa, Tomoyo
CORPORATE SOURCE: Fac. Med., Univ. Ryukyus, Okinawa, Japan
SOURCE: Pharmacology (1984), 29(4), 204-9
CODEN: PHMGBN; ISSN: 0031-7012
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 30 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Tracer-labeled l-[3H]-norepinephrine, d-[14C]**norephinephrine**, and d,l-[3H]-isoproterenol were infused simultaneously into patients with essential hypertension and into normotensive control subjects, in order to determine whether abnormalities in the disappearance kinetics of these substances characterized the hypertensive patients. The mean preinfusion venous plasma norepinephrine concentration was somewhat higher in the hypertensive group (260 vs. 194 pg/mL), but the groups did not differ in the disappearance kinetics of l- or d-norepinephrine or of isoproterenol. Preinfusion plasma norepinephrine was significantly pos. correlated with calculated spillover rates in both the hypertensive and normotensive groups, but not with norepinephrine clearances. The d/l ratio in plasma norepinephrine was the same as in the infusate during and after the infusion, even after pretreatment with the neuronal norepinephrine uptake blocker, desipramine. Because isoproterenol is not taken up by nerve endings, the ratio of [3H]isoproterenol to l-[3H]norepinephrine increased after the infusion ended. This increase was almost completely abolished by pretreatment with desipramine. Apparently, the increased plasma norepinephrine levels seen in some patients with essential hypertension result from increased sympathetic neural activity and not from decreased clearance of norepinephrine, changes in the isoproterenol/norepinephrine ratio after simultaneous infusion of both provide an index of neuronal norepinephrine uptake in man, and neuronal norepinephrine uptake is not stereospecific.

ACCESSION NUMBER: 1984:4252 CAPLUS
DOCUMENT NUMBER: 100:4252
TITLE: Plasma l-[3H]norepinephrine, d-[14C]norepinephrine, and d,l-[3H]isoproterenol kinetics in essential hypertension
AUTHOR(S): Goldstein, David S.; Horwitz, David; Keiser, Harry R.; Polinsky, Ronald J.; Kopin, Irwin J.
CORPORATE SOURCE: Natl. Heart, Lung, Blood Inst., Bethesda, MD, 20205, USA
SOURCE: Journal of Clinical Investigation (1983), 72(5), 1748-58
CODEN: JCINAO; ISSN: 0021-9738
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 31 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Harding-Passey mouse-melanoma tyrosinase (EC 1.14.18.1) is inhibited during L-DOPA oxidation by reaction products. L-3,4-Dihydroxyphenyl[3-14C]alanine oxidation products bind to the enzyme, as demonstrated by gel electrophoresis and radioactivity measurements. The enzyme interacts with indoles and oxidizes dopamine and **norephinephrine**. L-Epinephrine activates tyrosinase at nonhormonal concns., and bovine serum albumin protects the enzyme from autoinhibition. The inhibition of the Harding-Passey mouse-melanoma tyrosinase, during substrate oxidation, is very similar to that of the mushroom enzyme.

ACCESSION NUMBER: 1983:175466 CAPLUS
DOCUMENT NUMBER: 98:175466
TITLE: Harding-Passey mouse melanoma tyrosinase inactivation by reaction products and activation by L-epinephrine
AUTHOR(S): Miranda, Michele; Botti, Dario
CORPORATE SOURCE: Ist. Biol. Gen., Univ. Aquila, L'Aquila, 67100, Italy
SOURCE: General Pharmacology (1983), 14(2), 231-7
CODEN: GEPHDP; ISSN: 0306-3623
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 32 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

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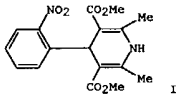

I

AB Mean arterial pressure was significantly decreased by nifedipine (I) [21829-25-4] in acute and chronic treatment in hypertensive patients, and the antihypertensive effect was enhanced by metoprolol [37350-58-6], mean arterial pressure did not change in controls in acute administration, while heart rate in these subjects was slower with added metoprolol. No significant change in heart rate was found with nifedipine, but patients in combined treatment had a lower heart rate. The plasma renin [9015-94-5] activity increase due to nifedipine was inhibited both in acute and in chronic treatment by the addition of metoprolol. Norepinephrine [51-41-2] showed a significant increase in both acute and chronic treatment with nifedipine, and the same pattern was shown with the combined treatment. Epinephrine [51-43-4] remained unchanged in all cases. The results confirm the effectiveness of nifedipine as an antihypertensive agent. This action was enhanced by metoprolol. The plasma renin activity stimulation due to nifedipine was reduced by metoprolol, while **norephinephrine** was only slightly affected. Nevertheless the combination of nifedipine with metoprolol seemed to reduce the sympathetic overactivity due to vasodilator alone. Apparently, antihypertensive therapy with combined drugs (nifedipine and metoprolol) is a safer, more effective, and rational treatment than the vasodilator alone.

ACCESSION NUMBER: 1980:597993 CAPLUS
DOCUMENT NUMBER: 93:197993
TITLE: Acute and long-term effects of nifedipine on plasma renin activity and plasma catecholamines in controls and hypertensive patients before and after metoprolol
AUTHOR(S): Corea, L.; Alunni, G.; Bentivoglio, M.; Boschetti, E.; Cosmi, F.; Giaimo, M. D.; Miele, N.; Motolese, M.
CORPORATE SOURCE: Ist. Semeiotica Med., Univ. Perugia, Perugia, Italy
SOURCE: Acta Therapeutica (1980), 6(2), 177-89
CODEN: ACTTDZ; ISSN: 0378-0619
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 33 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Palytoxin (PTX) [11077-03-5] caused a slow phasic contraction of the isolated guinea-pig vas deferens (2nd component) followed by the 1st rapid phasic contraction (1st component) at >3 + 10-9M. N-Acetylpalytoxin [73070-85-6] also produced similar actions but its potency was .apprx.1/100 of that of PTX. The 2nd component of PTX-induced contraction, but not the 1st component, was inhibited by treatments with phentolamine methanesulfonate [65-28-1], reserpine [50-55-5], and 6-hydroxydopamine [1199-18-4], but remained unaffected by atropine sulfate [55-48-1] and mecamylamine-HCl [826-39-1] pretreatment. Tetrodotoxin [4368-28-9] partially inhibited the 2nd component, whereas the 2nd component was inhibited by solns. low in Na+ (85.2 mM) or containing verapamil [52-53-9] (10-6M). Both components were abolished by high Mg or Ca-free medium. Thus, the 1st component was the result of a direct action of PTX on smooth muscle sites, whereas the 2nd phase was the result of an indirect action mediated through the **norephinephrine** bitartrate [51-40-1] release from the adrenergic nerve terminals.

ACCESSION NUMBER: 1980:526734 CAPLUS
DOCUMENT NUMBER: 93:126734
TITLE: Mechanism of the excitatory action of palytoxin and N-acetylpalytoxin in the isolated guinea-pig vas deferens
AUTHOR(S): Ohizumi, Y.; Shibata, S.
CORPORATE SOURCE: Sch. Med., Univ. Hawaii, Honolulu, HI, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1980), 214(1), 209-212
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 34 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB The reaction kinetics of norepinephrine N-methyltransferase (I) with m-octopamine-HCl (II) were compared with those for L-norepinephrine bitartrate (III). At high substrate concentration, excess II inhibited I activity. When the concentration of II was varied over a 25-400 μM range, however, linear kinetics were obtained with Km and Vmax values of 89 μM and 210 nmol/30 min, resp. Comparison of these values with those for III (concentration variation of 5-67 μμ) indicated that II has a lower affinity for I than does III. Nonetheless, II is methylated at a Vmax similar to that for III and, hence, the methylation of II may occur physiol. or after administration of II in the treatment of hypotension.

ACCESSION NUMBER: 1980:421557 CAPLUS
DOCUMENT NUMBER: 93:21557
TITLE: m-Octopamine as a substrate for norepinephrine N-methyltransferase
AUTHOR(S): Fuller, Ray W.; Hemrick, Susan K.
CORPORATE SOURCE: Lilly Res. Lab., Indianapolis, IN, 46285, USA
SOURCE: IRCS Medical Science: Library Compendium (1980), 8(5), 284
CODEN: IRLCDZ; ISSN: 0305-6651
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 35 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
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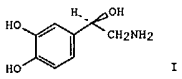

I

AB Rabbit aorta microsomes bound 3H-labeled l-norepinephrine (I) [51-41-2] to both high and low affinity sites. Both unlabeled d- and l-norepinephrine isomers equally displaced (20%) of the label from the binding site. The catechol-O-methyltransferase inhibitor inhibited binding by 80%, whereas the monoamine oxidase inhibitor pargyline inhibited binding by only 8.5%. With enzymic sites unrelated to receptor sites blocked by drugs it was determined that the high affinity site was capable of binding 10 pmoles I/mg microsomal protein and the dissociation constant was 1.2 + 10-6M. Binding of the α-antagonist dihydroergocryptine [25447-66-9] to bovine aorta microsomes was rapid and specific. Specific binding was saturable but represented only 21-9% of the total dihydroergocryptine binding to this preparation

ACCESSION NUMBER: 1978:574057 CAPLUS
DOCUMENT NUMBER: 89:174057
TITLE: Binding of adrenergic agonist L-(3H)-norepinephrine and antagonist (3H)-dihydroergocryptine to the microsomal fraction of beef and rabbit aorta
AUTHOR(S): Carman-Krzan, Marija
CORPORATE SOURCE: Med. Fac., Univ. Ljubljana, Ljubljana, Yugoslavia
SOURCE: Polish Journal of Pharmacology and Pharmacy (1978), 30(2-3), 281-92
CODEN: PJPPAA; ISSN: 0301-0244
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 36 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB 1,6-Di-O-(2-isocyano-3-methylcrotonyl)-D-mannitol (A32390A) [61241-59-6] is an isonitrile-containing derivative of diacyl D-mannitol. The compound is produced in fermentation as the major component of a metabolic complex known as A32390. A32390A inhibits dopamine-β-hydroxylase, reduces heart and adrenal **norephinephrine** levels, lowers blood pressure in hypertensive rats, and possesses antibiotic activity vs. gram-pos. bacteria and fungi. A32390 is produced in submerged culture by a mold, a species of Pyrenochaeta, NRRL-5786. Glucose and sucrose are among the best C sources for the biosynthesis of A32390. Mannitol, although a substituent of the A32390A mol., supports little or no biosynthesis of the compound when employed as the major C source for the fermentation The addition of crotonic acid derivs., EtOH, or L-histidine to the fermentation medium enhances the level of A32390 produced.

ACCESSION NUMBER: 1978:168438 CAPLUS
DOCUMENT NUMBER: 88:168438
TITLE: A32390A, a new biologically active metabolite. I. Discovery and fermentation studies
AUTHOR(S): Boeck, L. D.; Hoehn, M. M.; Sands, T. H.; Wetzel, R. W.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, USA
SOURCE: Journal of Antibiotics (1978), 31(1), 19-26
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 37 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB A fluorometric procedure is described for the determination of ng amts. of serotonin, norepinephrine, and dopamine in small brain areas (20-350 mg) from individual rats. The amines were separated from their precursor amino acids and acid metabolites by column chromatog. on Bio-Rex 70 (Na+-form, 200-400 mesh). It is possible quant. to determine 10-30 ng of each amine when all 3 are measured simultaneously. When either serotonin or the catecholamines are assayed in a tissue sample, ≥5-15 ng may be detected. Recoveries of the amines ranged 85-93% as measured by the addition of 14C-labeled amines to tissue supernatants.

ACCESSION NUMBER: 1978:148380 CAPLUS
DOCUMENT NUMBER: 88:148380
TITLE: Simultaneous determination of indole- and catecholamines in small brain regions in the rat using a weak cation exchange resin
AUTHOR(S): Holman, R. Bruce; Angwin, Pamela; Barchas, Jack D.
CORPORATE SOURCE: Dep. Psychiatr. Behav. Sci., Stanford Univ. Sch. Med., Stanford, CA, USA
SOURCE: Neuroscience (Oxford, United Kingdom) (1976), 1(2), 147-50
CODEN: NRSCDN; ISSN: 0306-4522
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 38 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB In the title method, 50 μL blood plasma or tissue extract was incubated with catechol O-methyltransferase and S-adenosylmethionine-3H. The catecholamines were converted to their O-methylated 3H-labeled derivs. These derivs. were purified by solvent extraction and were isolated by 1-dimensional silica gel thin-layer chromatograph. The spots containing the O-methylated derivs. were scraped directly into vials and were determined by liquid scintillation counting. Approx. 1 pg of each catecholamine could be measured with interassay relative standard deviations of 4.3, 8.9, and 13.2% for norepinephrine, epinephrine, and dopamine, resp. No cross-reactivity was noted for several compds. related to these catecholamines.

ACCESSION NUMBER: 1978:47203 CAPLUS
DOCUMENT NUMBER: 88:47203
TITLE: A simple specific radioenzymatic assay for the simultaneous measurement of picogram quantities of norepinephrine, epinephrine, and dopamine in plasma and tissues
AUTHOR(S): Sole, Michael J.; Hussain, M. Nasir
CORPORATE SOURCE: Dep. Med., Univ. Toronto, Toronto, ON, Can.
SOURCE: Biochemical Medicine (1977), 18(3), 301-7
CODEN: BIMDA2; ISSN: 0006-2944
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 39 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
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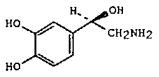

I

AB The effect of intraarterially administered norepinephrine-HCl (I-HCl) [329-56-6] on spinal cord blood flow (SCBF), before and after disruption of the blood-cord barrier was studied in dogs. Barrier disruption was accomplished with an intraarterial bolus injection of 2.5M urea. Multiple ligations of branches of the posterior aorta and cannula placements ensured that the urea was directed to the lumbar and sacral segments of the cord. Intraarterial urea by itself had no effect on SCBF. The intraarterial infusion of I (12 and 30 μg/min) was without overall effect on SCBF. However, if the blood-cord barrier had been previously disrupted with hypertonic urea, both concns. of I resulted in large decreases inSCBF. No such decreases in SCBF were seen with blood-cord barrier disruption and I if the animals had been pretreated with the α-blocker, phenoxybenzamine (1.5 mg/kg). Some aspects of the possible involvement of I in the pathophysiol. of acute spinal injury are discussed.

ACCESSION NUMBER: 1978:849 CAPLUS
DOCUMENT NUMBER: 88:849
TITLE: The effect of norepinephrine on the spinal cord circulation and its possible implications in the pathogenesis of acute spinal trauma
AUTHOR(S): Crawford, Robert A.; Griffiths, Ian R.; McCulloch, James
CORPORATE SOURCE: Wellcome Surg. Res. Inst., Glasgow, UK
SOURCE: Journal of Neurosurgery (1977), 47(4), 567-76
CODEN: JONSAC; ISSN: 0022-3085
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 40 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The GABA [56-12-2] agonist muscimol [2763-96-4] (0.44 nmol), the endogenous opiate receptor β-endorphin [60617-12-1] (1.46 nmol), and norepinephrine [51-41-2] (60 nmol) stimulated food intake in satiated rats when injected into the ventromedial hypothalamus. Eating induced by muscimol was inhibited by bicuculline, but not by naltrexone or phentolamine, whereas norepinephrine-induced eating was terminated by phentolamine and bicuculline; β-endorphin-induced eating was blocked by both naltrexone and bicuculline. The results implicate GABA in the regulation of food intake and suggest that it may be involved in the increased food intake induced by norepinephrine or opiate receptor agonists.

ACCESSION NUMBER: 1977:594490 CAPLUS
DOCUMENT NUMBER: 87:194490
TITLE: Stimulation of food intake by muscimol and beta endorphin
AUTHOR(S): Grandison, L.; Guidotti, A.
CORPORATE SOURCE: Lab. Preclin. Pharmacol, St. Elizabeth Hosp., Washington, DC, USA
SOURCE: Neuropharmacology (1977), 16(7-8), 533-6
CODEN: NEPHBW; ISSN: 0028-3908
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 41 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB In isolated guinea pig hearts perfused with Krebs-Henseleit solution (pH 7.4, 37°), coronary flow, contractile force, coronary sinus O levels, and adenosine [58-61-7] and its degradative products in perfusates were measured before and during the infusion of varying doses of L-epinephrine-HCl [55-31-2], l-norepinephrine bitartrate [51-40-1], histaminediphosphate [51-74-1], or nitroglycerin [55-63-0]. All 4 compds. produced increases in coronary flow. The catecholamines and histamine had a pos. inotropic effect, increased myocardial O consumption, and decreased coronary sinus O levels. The decrease in cornoary sinus O was accompanied by increased levels of adenosine in the perfusates. Nitroglycerin, on the other hand, did not change contractile force, increased coronary sinus O levels, and did not increase the rate of adenosine release. Changes in inosine [58-63-9] and hypoxanthine [68-94-0], degradative products of adenosine metabolism, paralleled those of adenosine in all expts. Apparently, adenosine release is intimately associated with a decrease of coronary sinus O levels.

ACCESSION NUMBER: 1977:512275 CAPLUS
DOCUMENT NUMBER: 87:112275
TITLE: Effects of catecholamines, histamine, and nitroglycerin on flow, oxygen utilization, and adenosine production in the perfused guinea pig heart
AUTHOR(S): Wiedmeier, Vernon, T.; Spell, Larry H.
CORPORATE SOURCE: Dep. Physiol., Med. Coll. Georgia, Augusta, GA, USA
SOURCE: Circulation Research (1977), 41(4), 503-8
CODEN: CIRUAL; ISSN: 0009-7330
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 42 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
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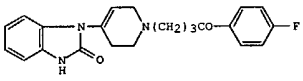

I

AB The effect of droperidol (I) [548-73-2] on the vasoconstriction induced by norepinephrine, sympathetic nerve stimulation, histamine and K ions was studied on isolated, perfused ear arteries; its effect on **norephinephrine**-induced contraction was studied on isolated aorta, spleen and vas deferens. In addition, the onset and duration of action of I was studied. Low doses of I inhibited the vasoconstriction induced by norepinephrine and sympathetic nerve stimulation in the ear artery of rabbit (3.3 + 10-γ M and 1.3 + 10-8 M respectively). At similar low doses, I inhibited norpinephrine-induced contractions in the other tissues studied and had a potency comparable to that of phentolamine; its action was rapid in onset and of short duration. High doses of I (10-6 M) also inhibited the vasoconstriction of the ear artery induced by histamine and by K ions. Thus, at low doses, I has specific and competitive α-adrenoceptor blocking effects.

ACCESSION NUMBER: 1977:495623 CAPLUS
DOCUMENT NUMBER: 87:95623
TITLE: Specific α-adrenoceptor blocking effect of droperidol on isolated smooth muscles
AUTHOR(S): Van Nueten, Jan M.; Reneman, Robert S.; Janssen, Paul A. J.
CORPORATE SOURCE: Dep. Pharmacol., Janssen Pharm., Beerse, Belg.
SOURCE: European Journal of Pharmacology (1977), 44(1), 1-8
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 43 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Pentobarbital (I) [57-33-0] (20-200μM, 180-s exposure) dose-dependently reduced the Ca-dependent efflux of both norepinephrine (II) [51-41-2] and GABA [56-12-2] from K-depolarized mouse forebrain synaptosomal fractions. I did not reduce either II or GABA release in the absence of Ca or the Ca-dependent release facilitated by A23187 [52665-69-7], but Ca-dependent release in the presence of K or veratridine [71-62-5] was depressed by I. The site of action of I in the stimulus-secretion coupling process may be the depolarization-triggered Ca permeation.

ACCESSION NUMBER: 1977:400118 CAPLUS
DOCUMENT NUMBER: 87:118
TITLE: Pentobarbital depression of stimulus-secretion coupling in brain. Selective inhibition of depolarization-induced calcium-dependent release
AUTHOR(S): Haycock, John W.; Levy, William B.; Cotman, Carl W.
CORPORATE SOURCE: Dep. Psychobiol., Univ. California, Irvine, CA, USA
SOURCE: Biochemical Pharmacology (1977), 26(2), 159-61
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 44 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

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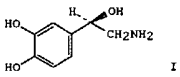

I

AB Effects of biogenic amines and peptides on urine outflow and antidiuretic hormone (AHD) [11000-17-2] release were studied using rat intracerebroventricular (i.c.v.) perfusion expts. and isolated rat neurohypophysis incubation studies. A decrease in the urine outflow was observed after norepinephrine bitartrate (I) [51-40-1], histamine-2HCl [56-92-8], and 5-valine-angiotensin II amide [53-73-6] were administered i.c.v. The effect of I was prevented by phentolamine mesylate [65-28-1]. Phentolamine alone also acted as an antidiuretic. When the isolated neurohypophysis was incubated in the presence of I, histamine, 5-valine-angiotensin II amide, or bradykinin [58-82-2], release of ADH was increased, and the effects of I and histamine were prevented by phentolamine and promethazine, resp. Phentolamine but not promethazine alone increased ADH release. On the other hand, serotonin, dopamine and 5-isoleucine-angiotensin II did not result in an ADH release from the isolated neural lobes. Apparently, when the local concentration of I, histamine, or peptides is increased to the extent where the posterior lobe of the pituitary is stimulated directly, the ADH release is enhanced.

ACCESSION NUMBER: 1977:183681 CAPLUS
DOCUMENT NUMBER: 86:183681
TITLE: Antidiuresis of centrally administered amines and peptides and release of antidiuretic hormone from isolated rat neurohypophysis
AUTHOR(S): Hisada, Shiro; Fujimoto, Seigo; Kamiya, Toshio; Endo, Yoshiko; Tsushima, Hiromi
CORPORATE SOURCE: Med. Sch., Nagoya City Univ., Nagoya, Japan
SOURCE: Japanese Journal of Pharmacology (1977), 27(1), 153-61
CODEN: JJPAAZ; ISSN: 0021-5198
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 45 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

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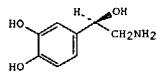

I

AB The effects of renal nerve stimulation (RNS) and norepinephrine (I) [51-41-2] infusion on the intrarenal distribution of renal blood flow were studied in the isolated blood-perfused canine kidney. Both RNS and I caused a redistribution of fractional blood flow from the inner half to the outer half of the renal cortex. Both vasoconstrictor stimuli resulted in a relatively greater vasoconstriction of the inner cortical vasculature. The inner cortical vasculature is apparently more responsive to vasoactive stimuli and may be the important locus for regulation of the distribution of renal cortical blood flow.

ACCESSION NUMBER: 1977:133908 CAPLUS
DOCUMENT NUMBER: 86:133908
TITLE: Redistribution of renal cortical blood flow by renal nerve stimulation and norepinephrine infusion
AUTHOR(S): Gotshall, R. W.; Itskovitz, H. D.
CORPORATE SOURCE: Sch. Med., Wright State Univ., Dayton, OH, USA
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1977), 154(1), 60-4
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 46 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Unavailable

ACCESSION NUMBER: 1977:69199 CAPLUS
DOCUMENT NUMBER: 86:69199
TITLE: 6-Hydroxydopamine depletion of brain norepinephrine lowers isolation-induced male mouse fighting behavior
AUTHOR(S): Crawley, Jacqueline N.
CORPORATE SOURCE: Univ. Maryland, College Park, MD, USA
SOURCE: (1976) 107 pp. Avail.: Xerox Univ. Microfilms, Ann Arbor, Mich., Order No. 76-27,372
From: Diss. Abstr. Int. B 1976, 37(6), 2705
DOCUMENT TYPE: Dissertation
LANGUAGE: English

L16 ANSWER 47 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Norepinephrine, but not dopamine, was increased in both the hypothalamus and telencephalon of genetically obese mice. In the telencephalon norepinephrine turnover time following α-methyl-p- tyrosine methyl ester administration was slower than that observed in the hypothalamus. For the obese mice the 95% confidence limits of the regression lines for hypothalamic and telencephalic norepinphrine did not overlap, suggesting a faster turnover time in the hypothalamus than in the telencephalon. This difference was not observed in lean littermates.

ACCESSION NUMBER: 1977:41230 CAPLUS
DOCUMENT NUMBER: 86:41230
TITLE: Central catechol amine turnover in genetically obese mice (obob)
AUTHOR(S): Lorden, Joan F.; Oltmans, Gary A.; Margules, David L.
CORPORATE SOURCE: Dep. Psychol., Temple Univ., Philadelphia, PA, USA
SOURCE: Brain Research (1976), 117(2), 357-61
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 48 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

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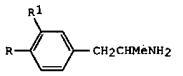


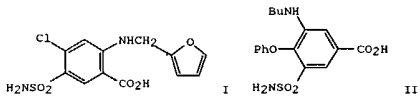
I, R=MeO, R^1=H
II, RR^1=OCH_2O

AB The ability of various drugs to prevent the lethal effects of 4-methoxyamphetamine-HCl (I-HCl) [3706-26-1] and 3,4-methylenedioxyamphetamine-HCl (II-HCl) [6292-91-7] were reduced by pretreatment with phentolamine mesylate [65-28-1] and 6-hydroxydopamine-HBr [636-00-0] suggesting that release of **norephinephrine** from peripheral adrenergic nerves contributed to their toxicity. Pretreatment with methysergide bimaleate [129-49-7] reduced the lethal effects of (+)-[51-63-8] and (-)-amphetamine sulfate [51-62-7], I, II, and 2,5-dimethoxy-4-methylamphetamine [15588-95-1] suggesting that an action on serotonergic receptors contributed to their toxicity. Pretreatment with 4-chloro-amphetamine, practolol and haloperidol did not alter the lethal effects of the agents studied.

ACCESSION NUMBER: 1976:516772 CAPLUS
DOCUMENT NUMBER: 85:116772
TITLE: The protective effects of methysergide, 6-hydroxydopamine and other agents on the toxicity of amphetamine, phentermine, MDA, PMA, and STP in mice
AUTHOR(S): Lopatka, J. E.; Brewerton, C. N.; Brooks, D. S.; Cook, D. A.; Paton, D. M.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Alberta, Edmonton, AB, Can.
SOURCE: Research Communications in Chemical Pathology and Pharmacology (1976), 14(4), 677-87
CODEN: RCOCB8; ISSN: 0034-5164
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 49 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

GI



I

II

AB Furosemide (I) [54-31-9] (10 or 40 μg/ml), bumetanide (II) [28395-03-1] (1 or 4 μg/ml), and indomethacin [53-86-1] (5 μg/ml) inhibited the pressor response of the rat mesenteric vascular bed to norepinephrine [51-41-2]; in each case responsiveness was restored by prostaglandin E2 [363-24-6]. I and II failed to inhibit responsiveness in the presence of an adequate amount (50 pg/ml) of prostaglandin E2. Ovine prolactin [9002-62-4] at a concentration of 50 ng/ml enhanced pressor responses to norepinephrine, but at 500 ng/ml inhibited responsiveness after an initial potentiation. Aspirin [50-78-2] (10 mg/ml), I, and II all reversed both potentiation produced by the lower prolactin concentration and the inhibition produced by the higher one. In light of previous findings, these results suggest that the diuretics exert their vascular effects by inhibiting prostaglandin synthesis, whereas prolactin acts by stimulating such synthesis.

ACCESSION NUMBER: 1976:472106 CAPLUS
DOCUMENT NUMBER: 85:72106
TITLE: Vascular actions of furosemide and bumetanide on the rat superior mesenteric vascular bed: interactions with prolactin and prostaglandins
AUTHOR(S): Mtabaji, J. P.; Manku, M. S.; Horrobin, D. F.
CORPORATE SOURCE: Dep. Physiol., Univ. Newcastle upon Tyne, Newcastle upon Tyne, UK
SOURCE: Canadian Journal of Physiology and Pharmacology (1976), 54(3), 357-66
CODEN: CJPPA3; ISSN: 0008-4212
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 50 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB A marked, reversible decline in cardiac **norephinephrine** stores was noted after exptl. myocardial infarction. Uptake and accumulation of tracer doses of DL-norepinephrine-7-14C, as well as the rate of degradation, appeared to be unchanged. Despite marked variation in pool size, the subcellular distribution appeared to be unchanged, and no preferential uptake into any subcellular fraction was observed

ACCESSION NUMBER: 1976:403555 CAPLUS
DOCUMENT NUMBER: 85:3555
TITLE: Metabolism of norepinephrine in noninfarcted heart muscle after experimental myocardial infarction
AUTHOR(S): Mathes, P.; Sack, D. W.; Gudbjarnason, S.
CORPORATE SOURCE: I. Med. Klin., Tech. Univ. Muenchen, Munich, Fed. Rep. Ger.
SOURCE: Recent Advances in Studies on Cardiac Structure and Metabolism (1976), 7(Biochem. Pharmacol. Myocardial Hypertrophy, Hypoxia, Infarction), 283-7
CODEN: RCSMCP; ISSN: 0363-5872
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 51 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Selective stimulation of the carotid body receptors in dogs by hypoxic, hypercapnic, acidotic blood (venous blood perfusion) produced bradycardia, an increase of coronary flow, and greater release of norepinephrine from the heart; the coronary resistances were decreased. The same stimulation after vagotomy was no longer accompanied by bradycardia. Under these conditions, the decrease of coronary resistance was less marked, and the release of **norephinephrine** was increased.

ACCESSION NUMBER: 1976:403326 CAPLUS
DOCUMENT NUMBER: 85:3326
TITLE: Carotid body control of coronary flow, myocardial oxidative metabolism, and cardiac catechol amines in the dog
AUTHOR(S): Limet, R.; Chabi, E.; Welch, K. M. A.; Kennedy, J. H.
CORPORATE SOURCE: Cora and Webb Mading Dep. Surg., Baylor Coll. Med., Houston, TX, USA
SOURCE: Recent Advances in Studies on Cardiac Structure and Metabolism (1976), 9(Sarcolemma), 269-78
CODEN: RCSMCP; ISSN: 0363-5872
DOCUMENT TYPE: Journal
LANGUAGE: English

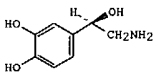
L16 ANSWER 52 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB In normally cycling women studied daily from day 10 to 17 of the menstrual cycle, the levels of circulating norepinephrine (I) showed a sharp rise preceding or concomitant with the ovulatory LH surge. In 2 of 3 patients the I peak took place 24 h before the LH rise; in the 3rd patient the I peak occurred simultaneously. The simultaneous determination of ovarian hormones and I showed no temporal correlation between I and either estradiol or progesterone. On the other hand, after a single i.v. 100 μg dose of LH-releasing hormone (LH-RH), a significant rise in plasma I, preceding the LH peak, was found in the patients studied. The determination of I at 3 min intervals beginning 1 min after LH-RH injection showed a significant rise in the I levels ranging 5-10 times higher than the basal values between 1 and 6 mins after LH-RH stimulation. In these patients a 2nd peak of I occurred simultaneously with the maximum response of LH, which rose to peak levels after 18 min in 1 patient and after 24 min in another. These findings are discussed with respect to the origin and role of increased amts. of plasma I related to the LH surge.

ACCESSION NUMBER: 1976:162530 CAPLUS
DOCUMENT NUMBER: 84:162530
TITLE: Plasma levels of norepinephrine (NE) during the periovulatory period and after LH-RH stimulation in women
AUTHOR(S): Rosner, Jorge M.; Nagle, C. A.; De Laborde, N. P.; Pedroza, E.; Badano, A.; Figueroa Casas, P. R.; Carril, M.
CORPORATE SOURCE: Inst. Latinoam. Fisiol. Reprod., Univ. Salvador, San Miguel, Argent.
SOURCE: American Journal of Obstetrics and Gynecology (1976), 124(6), 567-72
CODEN: AJOGAH; ISSN: 0002-9378
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 53 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

GI



I

AB In the absence of exogenously added neurotransmitters sympathetic denervation exerted little effect on the incorporation of 32P into the phospholipids of the excised rabbit iris muscle. In vivo the iris muscle incorporated 32P into phosphatidylinositol, phosphatidic acid, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine and sphingomyelin in that order of activity while in vitro phosphatidylinositol was followed by phosphatidylcholine. Tension responses of iris dilator muscle from dehydrated irises exhibited supersensitivity to **norephinephrine** (I) [51-41-2]. Furthermore, I at concns. of 3 μM and 30 mM produced 1.6 times and 3 times stimulation of the phosphatidic acid of the denervated muscle resp. In contrast at 30 μM it stimulated this phospholipid by 1.6 times in the normal muscle. This stimulation was completely blocked by phentolamine. Whereas in the normal muscle acetylcholine [51-84-3] stimulated the labeling of phosphatidic acid and phosphatidylinositol by more than 2 times, in the denervated muscle it only stimulated 1.4 to 1.7 times. Similarly when 32P was administered intracamerally, the labeling found in the various phospholipids of the denervated iris was significantly lower than that of the normal. Apparently, denervation decreases the 32P labeling in the presence of acetylcholine. The I-stimulated 32P incorporation into phosphatidic acid appears to be post-synaptic.

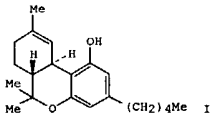
ACCESSION NUMBER: 1976:145150 CAPLUS
DOCUMENT NUMBER: 84:145150
TITLE: Effects of norepinephrine and acetylcholine on phosphorous-32 incorporation into phospholipids of the rabbit iris muscle following unilateral superior cervical ganglionectomy
AUTHOR(S): Abdel-Latif, Ata A.; Green, Keith; Matheny, James L.; McPherson, James C., Jr.; Smith, Jack P.
CORPORATE SOURCE: Dep. Cell Mol. Biol., Med. Coll. Georgia, Augusta, GA, USA
SOURCE: Life Sciences (1975), 17(12), 1821-8
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 54 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Isolated brown fat cells from hamster responded to added catechol amines with a temporary increase in respiratory rate and an extended lipolysis. From expts. with catechol amines and α and β-blockers, the receptors of these cells are classified as β according to classical definition. Norepinephrine [51-41-2] induced a rapid increase in cyclic-AMP [60-92-4] levels which paralleled in time the stimulated respiration. Maximum cyclic AMP levels were reached within 1-3 min and were followed by a continuous decline. Parallel to the catechol amine-induced respiration and lipolysis there was a pronounced drop in ATP [56-65-5] levels. This energy depletion was reversed by addition of the β-blocker propranolol within 5 min after **norephinephrine**. The nucleotide pattern in isolated hamster brown fat cells after norepinephrine addition was mimicked in expts. with isolated hamster brown fat mitochondria. A high ratio of AMP and ADP over ATP decreases the respiratory rate when endogenous free fatty acids are oxidized.

ACCESSION NUMBER: 1976:130560 CAPLUS
DOCUMENT NUMBER: 84:130560
TITLE: Norepinephrine-induced shift in levels of adenosine 3',5'-monophosphate and ATP parallel to increased respiratory rate and lipolysis in isolated hamster brown-fat cells
AUTHOR(S): Pettersson, Bertil; Vallin, Ivar
CORPORATE SOURCE: Wenner-Gren Inst., Univ. Stockholm, Stockholm, Swed.
SOURCE: European Journal of Biochemistry (1976), 62(2), 383-90
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 55 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
GI



I

AB Cardiovascular effects of Δ8- [5957-75-5] and Δ9-tetrahydrocannabinol (I) [1972-08-3] were studied after systemic i.v. administration and intra-arterial (i.a.) administration into a perfused vascular bed in the urethane-anesthetized rat. I.v. administration of the drugs produced dose-related transient increases in blood pressure followed by more prolonged hypotensive responses and bradycardia. Intra-arterial administration into the perfused hindquarters of the rat produced an increase in perfusion pressure indicative of vasoconstriction. The vasoconstrictor response to the cannabinoids corresponded temporally to a similar response produced by i.a. norepinephine bitartrate [51-40-1] and was in contrast in the more prolonged vasoconstrictor responses produced by vasopressin [11000-17-2]. Phentolamine, in a dose which reduced the vasoconstrictor effect of **norephinephrine** by 90%, significantly reduced the response to i.a. I while having no effect on the actions of i.a. vasopressin. Reserpine pretreatment significantly reduced vasoconstrictor actions of i.a. tyramine-HCl [60-19-5] and I but did not alter the responses to norepinephrine. These data suggest that the cannabinoids have peripheral vasoconstrictor activity in the rat which may be mediated, in part, through a tyramine-like action on adrenergic nerve terminals.

ACCESSION NUMBER: 1976:130421 CAPLUS
DOCUMENT NUMBER: 84:130421
TITLE: Vasoconstrictor actions of Δ8- and Δ9-tetrahydrocannabinol in the rat
AUTHOR(S): Adams, M. D.; Earnhardt, J. T.; Dewey, W. L.; Harris, L. S.
CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ., Richmond, VA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1976), 196(3), 649-56
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 56 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
GI For diagram(s), see printed CA Issue.
AB The lipolytic effect of norepinephrine (I) [51-41-2] in adipose tissue in vitro was studied before and after exercise in nonfasted rats with severe, untreated streptozotocin diabetes. I in increasing concns. stimulated glycerol release to an equal extent from the adipose tissue of nondiabetic and diabetic rats. However, the reesterification of free fatty acids (FFA) in adipose tissue was decreased by I in diabetic rats as compared to normal rats. During exercise, I further decreased the reesterification of FFA in adipose tissue of diabetic rats. Exercise did not change I-induced glycerol release in the adipose tissue of diabetic rats. In diabetic animals the increase in plasma glycerol and FFA during exercise was correlated inversely with the I-induced release of glycerol and FFA from the adipose tissue of the same animals after exercise. The lipolytic effect of I is not different in adipose tissue of diabetic and nondiabetic rats. By decreasing the reesterification of FFA, I is probably responsible for the observed increase in the release of FFA in vivo, a likely energy source in severely diabetic animals.

ACCESSION NUMBER: 1976:39060 CAPLUS
DOCUMENT NUMBER: 84:39060
TITLE: Influence of norepinephrine and exercise on lipolysis in adipose tissue of diabetic rats
AUTHOR(S): Koivisto, V. A.; Nikkila, E. A.; Akerblom, H. K.
CORPORATE SOURCE: Child. Hosp., Univ. Helsinki, Helsinki, Finland
SOURCE: Diabetologia (1975), 11(5), 401-5
CODEN: DBTGAJ; ISSN: 0012-186X
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 57 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Sinoaortic denervation (SAD) in the rabbit produced neurogenic hypertension which at 1st was characterized by increased cardiac output and later by increased peripheral vascular resistance. Tyrosine hydroxylase activity and catechol amine concentration of proximal mesenteric artery were greater than those of distal mesenteric vessels in normal rabbits. An hr after SAD **norephinephrine** (NE) synthesis, the activity of tyrosine hydroxylase assayed in vitro, was increased in proximal mesenteric artery and decreased in distal mesenteric vessels. Eleven and 30 days after SAD, NE synthesis in vivo and the activity of tyrosine hydroxylase assayed in vitro was increased in distal mesenteric vessels and decreased in proximal mesenteric artery. Sympathoadrenal regulation of increased splanchnic vascular resistance was an important factor in initiation and maintenance of neurogenic hypertension in the rabbit.

ACCESSION NUMBER: 1976:28917 CAPLUS
DOCUMENT NUMBER: 84:28917
TITLE: Altered norepinephrine synthesis of splanchnic vessels in neurogenic hypertension
AUTHOR(S): Dequattro, Vincent; Alexander, Natalie
CORPORATE SOURCE: Sch. Med., Univ. South. California, Los Angeles, CA, USA
SOURCE: European Journal of Pharmacology (1974), 26(2), 231-5
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 58 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
GI For diagram(s), see printed CA Issue.
AB The effects of 33 phenethylamines and phenethanolamines on uptake of norepinephrine [51-41-2] into cardiac tissue in vivo and release of norepinephrine from cardiac storage sites were determined The presence of m- or p-hydroxy substituents confers high inhibitory activity, while the o-hydroxy substituted compds. have little or no activity. Inhibitory and release activities were associated with the same general structural features. M-tyramine (I) [588-05-6] and m-octopamine (II) [536-21-0] were nearly equipotent, and among the most active inhibitors of norepinephrine uptake, while neither 6-hydroxynorepinephrine [2623-77-0] nor 6-hydroxyepinephrine [2623-79-2] were active. Structure-activity relations and binding mechanisms are discussed.

ACCESSION NUMBER: 1975:558496 CAPLUS
DOCUMENT NUMBER: 83:158496
TITLE: Norepinephrine uptake sites in cardiac tissue. Lack of affinity of 6-hydroxynorepinephrine and related compounds
AUTHOR(S): Rotman, A.; Lundstrom, J.; McNeal, E.; Daly, J.; Creveling, C. R.
CORPORATE SOURCE: Natl. Inst. Arthritis, Metab. Dig. Dis., Natl. Inst. Health, Bethesda, MD, USA
SOURCE: Journal of Medicinal Chemistry (1975), 18(2), 138-42
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 59 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
GI For diagram(s), see printed CA Issue.
AB The effect of norepinephrine (I) [51-41-2] on the intracellular H+ concentration
[H+]i of isolated rat hearts perfused with a modified Krebs-Henseleit solution (KHS) was determined The [H+]i was calculated with the [14C]-- dimethyloxazolidinedione method. Respiratory or metabolic acidosis was produced by equilibrating the KHS and 20% CO2 or decreasing the [HCO3-] of
the KHS, resp. Three types of expts. were carried out: (1) beta blockade-MJ 1999 (Sotalol) was added to the KHS, (2) control-no pharmacol.
treatment, and (3) I was added to the KHS. The effective CO2 buffer values (Δ[HCO3-]i/ΔpHi) during respiratory acidosis were: beta blockade 11, control 35, and I 84. The production of metabolic acidosis resulted in the following [H+]i changes: beta blockade 52 nM, control 60 nM, and I 7 nM. Apparently, I markedly attenuates the change in [H+]i accompanying respiratory and metabolic acidosis and may account in part for previous observations that the effective CO2 buffer value of cardiac muscle in vivo is greater than that in vitro.
ACCESSION NUMBER: 1975:526627 CAPLUS
DOCUMENT NUMBER: 83:126627
TITLE: Effect of norepinephrine on myocardial intracellular hydrogen ion concentration
AUTHOR(S): Riegle, K. M.; Clancy, R. L.
CORPORATE SOURCE: Med. Cent., Univ. Kansas, Kansas City, KS, USA
SOURCE: American Journal of Physiology (1975), 229(2), 344-9
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 60 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Daily oral administration of Pb [7439-92-1] to newborn rats had no adverse
effect on their body growth. Lead-treated rats were more active than age-matched controls. Endogenous levels of brain dopamine [51-61-6] were unchanged, whereas norepinephrine [51-41-2] was increased, suggesting a possible relationship between lead exposure during earliest developmental periods, increased motor activity, and brain **norephinephrine**, and not brain dopamine as previously postulated.
ACCESSION NUMBER: 1975:401644 CAPLUS
DOCUMENT NUMBER: 83:1644
TITLE: Growth, behavior, and brain catechol amines in lead-exposed neonatal rats. Reappraisal
AUTHOR(S): Golter, Marianne; Michaelson, I. Arthur
CORPORATE SOURCE: Coll. Med., Univ. Cincinnati, Cincinnati, OH, USA
SOURCE: Science (Washington, DC, United States) (1975), 187(4174), 359-61
CODEN: SCIEAS; ISSN: 0036-8075
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 61 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB A procedure for measuring pg quantities of norepinephrine was developed that used partially-purified bovine adrenal phenylethanolamine-N-methyl-transferase and 3H-labeled S-adenosylmethionine. The sensitivity of the assay was 25 pg, and the procedure was applicable to many body tissues and
fluids, including brain and blood plasma.
ACCESSION NUMBER: 1975:121212 CAPLUS
DOCUMENT NUMBER: 82:121212
TITLE: Sensitive radioenzymic assay for norepinephrine in tissues and plasma
AUTHOR(S): Henry, David P.; Starman, Barbra J.; Johnson, David G.; Williams, Robert H.
CORPORATE SOURCE: Sch. Med., Univ. Washington, Seattle, WA, USA
SOURCE: Life Sciences (1975), 16(3), 375-84
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 62 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Male subjects (19-23 years old) underwent a 7-day control period with respect to diet, temperature (22°), and sleep (7.5 hr), followed by a 2-day exposure to 15° and a 2-day recovery period (22°). Urine was collected every 8 hr commencing at 2300 hr and assayed for MHPG and VMA using gas-liquid chromatog. During the control period a diurnal rhythmicity was demonstrated for MHPG and VMA with maxima at 0700-1500 hr.
The mean excretory rates for MHPG and VMA were 0.71 and 2.6 μg/mg creatinine, resp. Cold exposure abolished the rhythms for MHPG and VMA and caused an 18% increase in MHPG excretion. In contrast, VMA excretion was not altered. Significant correlations were obtained with MHPG excretion and both urinary cortisol and rectal temperature MHPG excretion may
be indicative of changes in **norephinephrine** metabolism in the central nervous system, although alterations in peripheral degradative pathways cannot be ruled out.
ACCESSION NUMBER: 1975:109619 CAPLUS
DOCUMENT NUMBER: 82:109619
TITLE: Alteration of circadian rhythmicities of urinary 3-methoxy-4-hydroxyphenylglycol (MHPG) and vanilmandelic acid (VMA) in man during cold exposure
AUTHOR(S): Cymerman, Allen; Francesconi, Ralph F.
CORPORATE SOURCE: Mil. Stress Lab., U. S. Army Res. Inst. Environ. Med.,
Natick, MA, USA
SOURCE: Life Sciences (1975), 16(2), 225-36
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 63 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Unavailable
ACCESSION NUMBER: 1975:96057 CAPLUS
DOCUMENT NUMBER: 82:96057
TITLE: Inhibition of sacral parasympathetic preganglionic neurons by GABA, glycine, 5-hydroxytryptamine, and **norephinephrine**
AUTHOR(S): Thomson, Thomas D.
CORPORATE SOURCE: Univ. Utah, Salt Lake City, UT, USA
SOURCE: (1974) 82 pp. Avail.: Xerox Univ. Microfilms, Ann Arbor, Mich., Order No. 74-25,998
From: Diss. Abstr. Int. B 1974, 35(6), 2931
DOCUMENT TYPE: Dissertation
LANGUAGE: English

L16 ANSWER 64 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Uptake of norepinephrine-3H by slices of the hypothalamus and medial lower brainstem of rats exhibited a significant rhythm with respect to the circadian stage at which the rats were killed. In both regions, the daily min. uptake was about the same and the time of daily maximum was also about the same. The maximum uptake occurred in slices prepared 1 hr after the start of the dark phase. However, the amplitude of the circadian increase in uptake was greater and the circadian decrease in uptake occurred more slowly in the hypothalamus than in the brainstem. The rises above the daily min. were 25 and 20% in the former and the latter regions, resp. The min. in norepinephrine-3H uptake occurred 2 hr after the start of the light phase for the hypothalamus, whereas in the brainstem it occurred at the middle of the dark phase. Thus, ≥1 components of the uptake or accumulation of norepinephrine show circadian rhythm, and circadian changes in **norephinephrine** synthesis are probably not sufficient to explain the rhythm in brain region norepinephrine content.
ACCESSION NUMBER: 1975:70991 CAPLUS
DOCUMENT NUMBER: 82:70991
TITLE: Twenty-four-hour rhythmic uptake of tritium-labeled norepinephrine in vitro by hypothalamus and medial lower brainstem
AUTHOR(S): Lew, G. M.; Quay, W. B.
CORPORATE SOURCE: Dep. Zool., Univ. California, Berkeley, CA, USA
SOURCE: International Journal of Chronobiology (1974), 2(2), 209-13
CODEN: IJCBAU; ISSN: 0300-9998
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 65 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Long-term regulation of the cyclic AMP phosphodiesterase [9036-21-9] of the C-6 rat glioma cell line has been studied. Both the low Km and high Km activities were induced by elevation of intracellular cyclic AMP [60-92-4] levels following either dibutyryl cyclic AMP [362-74-3] or norepinephrine [51-41-2] treatment of the cells. The presence of either cycloheximide or actinomycin D prevented induction by either dibutyryl cyclic AMP or norepinephrine. Evidence was presented that the norepinephrine effect is mediated by the β-catecholamine receptor. The increased phosphodiesterase activity caused a partial refractoriness to a second challenge with norepinephrine, which could be overcome by blockade of the induction with cycloheximide. Apparently, just as short-term regulation of cyclic AMP levels occurs via changes in the rates of synthesis or degradation, long-term alterations of the system may also involve either the adenylate cyclase or the phosphodiesterase.
ACCESSION NUMBER: 1975:68555 CAPLUS
DOCUMENT NUMBER: 82:68555
TITLE: Cyclic AMP-mediated induction of the cyclic AMP phosphodiesterase of C-6 glioma cells
AUTHOR(S): Schwartz, Joan P.; Passonneau, Janet V.
CORPORATE SOURCE: Natl. Inst. Neurol. Dis. Stroke, Natl. Inst. Health, Bethesda, MD, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1974), 71(10), 3844-8
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 66 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The regulatory influence of thyroid hormone on norepinephrine(I) and its synthesizing enzyme, tyrosine hydroxylase(II), was investigated in developing rat brain. The appearance of brain II was preceded by that of I, since II had attained 75% of adult values 7 days after birth, when the concentration of I was only .apprx.40%. Exptl. cretinism, induced by a single i.p. injection of 200 μCi of 131I on the day of birth, led to an impairment of the normal developmental increases in the activity of II and brain I. Whereas 50 μCi of 131I exerted only little effect, 200 μCi inhibited the ontogenic increases in II activity by 31% and in I by 34%. When the radiothyroidectomy was delayed for 20 days, smaller decreases were observed in brain I and II. Treatment of neonatally thyroidectomized rats with L-triiodothyronine early in life restored the neurochem. changes in I metabolism in both a time- and dose-dependent manner. When the initiation of L-triiodothyronine treatment was delayed until adulthood, this hormone failed to produce any appreciable change in brain I and II. A critical period apparently exists in early postnatal life during which thyroid hormone is essential for the normal development of brain I metabolism The depressed behavior of hypothyroid rats may be related to reduced levels of I at the postsynaptic regions.
ACCESSION NUMBER: 1975:41129 CAPLUS
DOCUMENT NUMBER: 82:41129
TITLE: Alterations in brain norepinephrine and tyrosine hydroxylase activity during experimental hypothyroidism in rats
AUTHOR(S): Rastogi, Ram B.; Singhal, Radhey L.
CORPORATE SOURCE: Dep. Pharmacol., Univ. Ottawa, Ottawa, ON, Can.
SOURCE: Brain Research (1974), 81(2), 253-66
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 67 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Noradrenaline regulated thermogenesis during cold adaptation in rats via an effect on β-adrenergic receptors.
ACCESSION NUMBER: 1974:533876 CAPLUS
DOCUMENT NUMBER: 81:133876
TITLE: Noradrenaline and adaptation to cold
AUTHOR(S): Pastukhov, Yu. F.
CORPORATE SOURCE: Inst. Biol. Probl. Severa, Magadan, USSR
SOURCE: Sb. Mater. Nauch. Konf. Fiziol., Biokhim. Farmakol. Zapad.-Sib. Ob'edin., 5th (1973), Meeting Date 1972, 140-1. Editor(s): Larin, E. F. Tomsk. Gos. Univ.: Tomsk, USSR.
CODEN: 28LYAB
DOCUMENT TYPE: Conference
LANGUAGE: Russian

L16 ANSWER 68 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB With the possible exception of a slight enhancement of release, neither acute nor chronic administration of synthetic thyrotropin releasing hormone (TRH) [24305-27-9] (8 mg/kg, i.p.) had any effect on the disposition and metabolism of 3H-labeled norepinephrine [51-41-2] in rat brain. In addition, no significant changes were found in brain levels of endogenous norepinephrine, serotonin [50-67-9], or dopamine [51-61-6] following the injection of TRH. Thus, little evidence was found to support a possible relation between the reported clin. antidepressant activity of TRH and its effects on **norepinephrine** metabolism in the brain.
ACCESSION NUMBER: 1974:486363 CAPLUS
DOCUMENT NUMBER: 81:86363
TITLE: Norepinephrine metabolism in the rat brain following acute and chronic administration of thyrotropin releasing hormone
AUTHOR(S): Reigle, Thomas G.; Avni, Jacob; Platz, Patricia A.; Schildkraut, Joseph J.; Plotnikoff, Nicholas P.
CORPORATE SOURCE: Dep. Psychiatry, Harvard Med. Sch., Boston, MA, USA
SOURCE: Psychopharmacologia (1974), 37(1), 1-6
CODEN: PSYPAG; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 69 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Nictitating membrane contractile responses to i.v. infused l-norepinephrine bitartrate (I) [51-40-1] were increased by denervation (removal of nodose and superior cervical ganglia) or decentralization (removal of a piece of the cervical trunk and vagus). Dose-response data indicated that differences in the degree of decentralization or denervation supersensitivity obtained with I in previous in vivo and in vitro expts. are dependent on whether steady-state or nonsteady-state responses are measured.
ACCESSION NUMBER: 1974:433734 CAPLUS
DOCUMENT NUMBER: 81:33734
TITLE: Sensitivity of the nictitating membrane of the pithed cat to infusions of l-norepinephrine after denervation or decentralization
AUTHOR(S): Tsai, T. H.; Kuhn, W. L.
CORPORATE SOURCE: Merrell-Natl. Lab. Div., Richardson-Merrell, Inc., Cincinnati, OH, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1974), 188(3), 630-9
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 70 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB A study was done on K uptake and spontaneous rate of discharge in Purkinje fibers from canine hearts perfused in a tissue bath in close proximity to a β-probe. Norepinephrine-induced K uptake was unaffected by lack of O or glucose but was blocked when the energy supply to the Na-K pump or the activity of the pump itself was interfered with by 2-deoxy-D-glucose, low temperature, lack of Mg, strophanthidin, lack of Na, or tetrodotoxin. Norepinephrine apparently increases K uptake by stimulating active transport. In addition, the stimulatory action of **norepinephrine** on K uptake can be dissociation from its stimulatory action on Purkinje fiber automaticity.
ACCESSION NUMBER: 1974:423701 CAPLUS
DOCUMENT NUMBER: 81:23701
TITLE: Effects of norepinephrine on active potassium ion transport and automaticity in cardiac Purkinje fibers
AUTHOR(S): Borasio, P. G.; Vassalle, Mario
CORPORATE SOURCE: Dep. Physiol., State Univ. New York, Brooklyn, NY, USA
SOURCE: Recent Advances in Studies on Cardiac Structure and Metabolism (1974), 4, 41-57
CODEN: RCSMCP; ISSN: 0363-5872
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 71 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The β2 blocking agent N-isopropylmethoxamine (I) [550-53-8] (10-8-10-4 M) significantly antagonized the depressant activity of isoproterenol [7683-59-2], epinephrine [51-43-4], and **norephinephrine** [51-41-2] on the motility of isolated rabbit detrusor muscle strips, while the β1 blocker, practolol [6673-35-4] (10-8-10-4 M), tended to augment the depressive effects. The data suggested the β receptors of the rabbit detrusor resembled more closely the β2 type than the β1 type.

ACCESSION NUMBER: 1974:409752 CAPLUS
DOCUMENT NUMBER: 81:9752
TITLE: Selective beta blockade of isolated rabbit detrusor muscle with practolol (AY 21011) and N-isopropylmethoxamine
AUTHOR(S): Anderson, G. F.; Kreulen, D. L.; Fredericks, C. M.
CORPORATE SOURCE: Sch. Med., Wayne State Univ., Detroit, MI, USA
SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1973), 205(2), 373-80
CODEN: AIPTAK; ISSN: 0003-9780
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 72 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The pressor effect of 2-amino-5-(3,4-dichlorophenoxymethyl)-2-oxazoline (I) [51230-28-5] in dogs was less than that of d-amphetamine sulfate [51-63-8]. Upon repeated administration, tachyphylaxis developed to its pressor but not to its depressor effect. The pressor effect of I was antagonized by pretreatment with reserpine phosphate [1263-94-1] or with phenoxybenzamine-HCl [63-92-3]. I appears to act indirectly through the release of **norephinephrine** [51-41-2] from peripheral nerve endings. Spinalectomy did not significantly affect its pressor activity suggesting that the brain is not involved in its pressor effect. I had a biphasic action on blood pressure; a depressor activity followed by a pressor activity.

ACCESSION NUMBER: 1974:409726 CAPLUS
DOCUMENT NUMBER: 81:9726
TITLE: Cardiovascular activity of 2-amino-5-(3,4-dichlorophenoxymethyl)-2-oxazoline (APMO)
AUTHOR(S): Abdallah, A. H.; White, H. D.
CORPORATE SOURCE: Chem. Biol. Res., Dow Chem. Co., Midland, MI, USA
SOURCE: Toxicology and Applied Pharmacology (1973), 26(4), 513-22
CODEN: TXAPA9; ISSN: 0041-008X
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 73 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Incubation of isolated rat epididymal fat cells with 0.2 or 10 nM insulin [9004-10-8] decreased the level of cyclic AMP (I) [60-92-4] in the presence or absence of various lipolytic agents except in the presence of high concns. of catechol amines (0.1-1 mM). When the cells were incubated with 0.01-100 nM insulin, it gave: (a) a biphasic inhibitory effect that was maximal between 0.1 and 1 nM and submaximal at either higher or lower insulin concns on lipolysis stimulated by 0.5 mM dibutyryl I, 10 nM ACTH [9002-60-2], or 1-10 μM norepinephrine [51-41-2]; (b) a monophasic inhibitory effect that was maximal at 1-100 nM on lipolysis induced by 5-20 mM I or 1-4 mM caffeine; and (c) a monophasic stimulatory effect that was maximal at 10-100 nM on lipolysis induced by 1 mM dibutyryl I or 0.1-1 mM **norephinephrine**. Since the insulin inhibitory and stimulatory lipolytic effects seem to be mediated by the cellular insulin receptor or receptors, and not necessarily by decreased I levels, it appears that the insulin receptor system of fat cells can respond to a wide concentration range of the hormone.

ACCESSION NUMBER: 1974:141243 CAPLUS
DOCUMENT NUMBER: 80:141243
TITLE: Effects of insulin on the levels of adenosine 3',5'-monophosphate and lipolysis in isolated rat epididymal fat cells
AUTHOR(S): Kono, Tetsuro; Barham, Frances, W.
CORPORATE SOURCE: Sch. Med., Vanderbilt Univ., Nashville, TN, USA
SOURCE: Journal of Biological Chemistry (1973), 248(21), 7417-26
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 74 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB In doca-salt hypertensive rats and spontaneously hypertensive rats the norepinephrine (I) turnover of peripheral and central adrenergic neurons was determined by measuring the rate of decline of endogenous I after inhibition of tyrosine hydroxylase or by measuring the decay of the specific activity after labeling the stores by i.v. or intraventricular injection of [3H]-I. In the 2 types of hypertensive rats turnover in the periphery was delayed in proportion to the rise in systolic blood pressure, whereas in brain stem and residual parts of the brain the I turnover did not differ from that of normotensive controls. In doca-salt hypertension the cardiac I turnover was enhanced in proportion to the rise in blood pressure and reciprocally delayed in brain-stem (medulla-pons, hypothalamus) but not residual parts of the brain. Administration of chlorisondamine, a ganglion-blocking agent which does not cross the blood-brain barrier, resulted in a normalization of both blood pressure and cardiac I turnovers, whereas the changes in brain persisted. Encapsulation of the kidney and implantation of doca alone produced neither a rise in blood pressure nor changes in I turnover. It is concluded that in this form of exptl. hypertension the changes in I turnover in the brain stem is casually related to the increased activity of the peripheral sympathetic nervous system which normally is depressed by the activity of the adrenergic neurons in the brain stem. In spontaneously hypertensive rats neither the peripheral nor the central adrenergic nervous system seems to play a primary role in the development of hypertension. The delay in the peripheral I turnover, which is the biochem. correlate of a decreased sympathetic activity, may represent an attempt to compensate for an increased peripheral resistance resulting from changes in the reactivity of vascular smooth muscles or changes in vascular geometry.

ACCESSION NUMBER: 1974:13412 CAPLUS
DOCUMENT NUMBER: 80:13412
TITLE: Doca [deoxycorticosterone acetate]-salt and spontaneously hypertensive rats. Comparative studies on norepinephrine turnover in central and peripheral adrenergic neurons
AUTHOR(S): Nakamura, Keiji; Gerold, Marcel; Thoenen, Hans
CORPORATE SOURCE: Lab. Exp. Med., F. Hoffmann-La Roche Und Co., Basel, Switz.
SOURCE: Spontaneous Hypertension (1972), 51-8. Editor(s): Okamoto, Kozo. Igaku Shoin Ltd.: Tokyo, Japan.
CODEN: 27GTAW
DOCUMENT TYPE: Conference
LANGUAGE: English

L16 ANSWER 75 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Brain norepinephrine metabolism and catechol amine synthesis were measured in rats subjected to elec. footshock in the presence or absence of another subject. Animals shocked in pairs engaged in fighting behavior, whereas animals receiving shock without another rat present could not fight. Marked differences in the metabolism of norepinephrine formed from intracisternally injected dopamine 3-H were found in the 2 groups receiving footshock. Within each exptl. group, alterations in norepinephrine metabolism showed anatomic specificity, and temporal effects on metabolism in various brain regions were observed at various intervals following presentation of footshock. The observed changes in norepinephrine metabolism suggest that in rats receiving footshock without a partner, catechol amine turnover in the medulla-pons specifically increases during the shock period. In contrast, rats shocked in pairs, thereby eliciting fighting responses, show no alterations in regional norepinephrine metabolism during the period of shock.

ACCESSION NUMBER: 1974:1864 CAPLUS
DOCUMENT NUMBER: 80:1864
TITLE: Brain norepinephrine metabolism and shock-induced fighting behavior in rats. Differential effects of shock and fighting on the neurochemical response to a common footshock stimulus
AUTHOR(S): Stolk, Jon M.; Conner, Robert L.; Levine, Seymour; Barchas, Jack D.
CORPORATE SOURCE: Dep. Psychiatry, Stanford Univ., Stanford, CA, USA
SOURCE: U. S. Nat. Tech. Inform. Serv., AD Rep. (1973), No. 764072, 60 pp. Avail.: NTIS
From: Govt. Rep. Announce. (U.S.) 1973, 73(18), 30
CODEN: XADRCH
DOCUMENT TYPE: Report
LANGUAGE: English

L16 ANSWER 76 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Intraventricularly administered dopamine [51-61-6] (200-800 μg) and apomorphine [58-00-4] (10-80 μg) decreased the rearing response in rats but caused a dose-dependent increase in ambulation. Intraventricular **norephinephrine** [51-41-2] (2-64 μg) and clonidine [4205-90-7] (2-64 μg) decreased both ambulation and rearing. Thus, dopaminergic, but not noradrenergic receptors in the brain appear to be involved in stereotyped behavior.

ACCESSION NUMBER: 1973:532917 CAPLUS
DOCUMENT NUMBER: 79:132917
TITLE: Effect of substances acting on the central adrenergic receptor on open field behavior in rats
AUTHOR(S): Dandiya, P. C.; Patni, S. K.
CORPORATE SOURCE: Dep. Pharmacol., S.M.S. Med. Coll., Jaipur, India
SOURCE: Indian Journal of Medical Research (1913-1988) (1973), 61(6), 891-5
CODEN: IJMRAQ; ISSN: 0019-5340
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 77 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB In the vagotomized dog, the sinus acceleration induced by perfusion of the sinus node artery with 1μg of dopamine [51-61-6] or 0.1μg of norepinephrine [51-41-2] was suppressed by 30-100μg of haloperidol (I) [52-86-8]. I showed no differentiation of blocking activity between dopamine- and norepinephrine-induced positive chronotropic effects. Injection of nore than 100 μg of I frequently caused sinus arrhythmia.

ACCESSION NUMBER: 1973:511750 CAPLUS
DOCUMENT NUMBER: 79:111750
TITLE: Effect of haloperidol on sinus acceleration responses to dopamine and norepinephrine
AUTHOR(S): Chiba, Shigetoshi; Satoh, Keisuke; Hashimoto, Koroku
CORPORATE SOURCE: Sch. Med., Tohoku Univ., Sendai, Japan
SOURCE: Tohoku Journal of Experimental Medicine (1973), 110(2), 207-8
CODEN: TJEMAO; ISSN: 0040-8727
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 78 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Alpha-blockade virtually abolished the pulmonary pressor responses to hypoxia, hypercapnic acidosis, histamine, and **norephinephrine**, but did not produce reversal of the pressor response (i.e. vasodilation) to these agents. Reversal of the pulmonary pressor response to epinephrine occurred after alpha-blockade, but the vasodilation was slight and consistent with previous observations of meager vasodilations with isoproterenol without blockade. It is suggested that beta-adrenergic mechanisms are not only relatively scarce in the pulmonary circulation but also are not directly stimulated by hypoxia, hypercapnic acidosis, or histamine. Enhanced pulmonary pressor responses to hypoxia, hypercapnia, and histamine occurred during beta-blockade and may be due to the unmasking of addnl., but previously antagonized, alpha-receptors. Since no significant effect on the pressor response to serotonin was evident from either alpha- or beta-blockade, a different mechanism mediating the pressor response to this agent is suggested.

ACCESSION NUMBER: 1973:430033 CAPLUS
DOCUMENT NUMBER: 79:30033
TITLE: Adrenergic receptors in pulmonary vasoconstrictor responses to gaseous and humoral agents
AUTHOR(S): Porcelli, Robert J.; Bergofsky, Edward H.
CORPORATE SOURCE: Sch. Med., New York Univ., New York, NY, USA
SOURCE: Journal of Applied Physiology (1948-1976) (1973), 34(4), 483-8
CODEN: JAPYAA; ISSN: 0021-8987
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 79 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB In pithed rats, the potentiation of the pressor response to exogenous or endogenous norepinephrine [51-41-2] by the catechol-o-methyltransferase (COMT) inhibitor, pyrogallol [87-66-1], was enhanced by desipramine-HCl [58-28-6]. In the presence of desipramine, pyrogallol also increased the uptake of **norephinephrine**-3H by the heart. Thus, the participation of COMT in norepinephrine inactivation must be greater when norepinephrine uptake is inhibited by a potent catechol amine uptake inhibitor, such desipramine.

ACCESSION NUMBER: 1973:427374 CAPLUS
DOCUMENT NUMBER: 79:27374
TITLE: Modification by desipramine of the pyrogallol adrenergic sensitization in the rat
AUTHOR(S): Caillard, C.; Rapin, J. R.; Bralet, J.; Rossignol, P.
CORPORATE SOURCE: Lab. Pharmacodyn., U.E.R. Sci. Pharm. Biol., Paris, Fr.
SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1973), 202(1), 153-62
CODEN: AIPTAK; ISSN: 0003-9780
DOCUMENT TYPE: Journal
LANGUAGE: French

L16 ANSWER 80 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Acetylcholine chloride [60-31-1] (5 .tim. 10-8-5 .tim. 10-7 g/ml depressed the contractions and diminished the efflux of tritiated norepinephrine [51-41-2] induced by elec. stimulation of canine saphenous vein strips in vitro. Thus, acetylcholine relaxes venous smooth muscle during sympathetic stimulation by inhibiting the release of norepinephrine from the nerve endings.

ACCESSION NUMBER: 1973:413435 CAPLUS
DOCUMENT NUMBER: 79:13435
TITLE: Inhibition of tritium labeled **norephinephrine** release from sympathetic nerve endings in veins by acetylcholine
AUTHOR(S): Vanhoutte, Paul M.; Lorenz, Robert R.; Tyce, Gertrude M.
CORPORATE SOURCE: Mayo Clin. and Mayo Found., Rochester, MN, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1973), 185(2), 386-94
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 81 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB A daily rhythm in norepinephrine (I) content was demonstrated in the brain-stem, diencephalon, and cerebral cortex of hamsters (Mesocricetus auratus), exposed to a 12/12-hr light-dark cycle for a month or longer and then sacrificed at intervals over a 24-hr period. The rhythms in brain-stem and cerebral cortex were reproducible, with the peak in I content in each area occurring during the late light phase. The I rhythm in the brain-stem was demonstrated when different methods for I extraction were utilized.

ACCESSION NUMBER: 1973:157337 CAPLUS
DOCUMENT NUMBER: 78:157337
TITLE: Daily rhythm in norepinephrine content in regions of the hamster brain
AUTHOR(S): Morgan, William M.; McFadin, Linda S.; Harvey, Catherine Y.
CORPORATE SOURCE: Med. Sch., Univ. Texas, San Antonio, TX, USA
SOURCE: Comparative and General Pharmacology (1973), 4(13), 43-8
CODEN: CPGPAY; ISSN: 0010-4035
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 82 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN

AB Application of indomethacin, a drug known to inhibit prostaglandin synthesis, to isolated perfused rabbit hearts decreased the release of prostaglandins normally induced by nerve stimulation and simultaneously increased the release of norepinephrine in response to nerve stimulation. Indomethacin itself did not affect norepinephrine release from the heart in the absence of nerve stimulation nor did it affect the uptake of exogenous **norephinephrine**, suggesting that the increased norepinephrine release reflects disinhibition of a feedback mechanism, using endogenously formed prostaglandins for limitation of norepinephrine release.

ACCESSION NUMBER: 1973:41031 CAPLUS
DOCUMENT NUMBER: 78:41031
TITLE: Augmented noradrenaline release following nerve stimulation after inhibition of prostaglandin synthesis with indomethacin
AUTHOR(S): Junstad, Marianne; Pham Huu Chanh; Wennmalm, Ake
CORPORATE SOURCE: Dep. Physiol., Karolinska Inst., Stockholm, Swed.
SOURCE: Acta Physiologica Scandinavica (1972), 86(4), 563-7
CODEN: APSCAX; ISSN: 0001-6772
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 83 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB In anesthetized cats, endogenous norepinephrine [51-41-2], epinephrine [51-43-4], and dopamine [51-61-6] released from the adrenal medulla and sympathetic nerve endings inhibited transmission in the stellate ganglion.
The actions of these catechol amines were inhibited by adrenergic α-receptor blockade. Isoproterenol [7683-59-2] increased the ganglionic transmission but this action was inhibited by β-receptor blockade. The preganglionic nerve stimulation in the stellate ganglion produced an increase in left intraventricular pressure but this response was depressed by topical application of norepinephrine to the stellate ganglion.
ACCESSION NUMBER: 1973:24372 CAPLUS
DOCUMENT NUMBER: 78:24372
TITLE: Effects of catechol amines on sympathetic evoked action potentials in the stellate ganglion of the cat
AUTHOR(S): Sakanashi, Matao
CORPORATE SOURCE: Med. Sch., Kumamoto Univ., Kumamoto, Japan
SOURCE: Japanese Journal of Pharmacology (1972), 22(3), 391-401
CODEN: JJPAAZ; ISSN: 0021-5198
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 84 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB A new method was developed for the determination of amines and amine turnover in
tissues using gas chromatog. followed by mass spectral fragmentation of the effluent products. The method was applied to catechol amines in rat ganglia. Reserpine (I) [50-55-5] (0.1 and 0.5 mg/kg) depleted norepinephrine [51-41-2] by 82 and 92%, resp. In contrast, the dopamine [51-61-6] levels were unchanged and decreased 55%, resp.
ACCESSION NUMBER: 1973:256 CAPLUS
DOCUMENT NUMBER: 78:256
TITLE: Gas chromatography-mass fragmentography. New approach
to the estimation of amines and amine turnover
AUTHOR(S): Cattabeni, F.; Koslow, S. H.; Costa, E.
CORPORATE SOURCE: Saint Elizabeths Hosp., Washington, DC, USA
SOURCE: Advances in Biochemical Psychopharmacology (1972), 6, 37-59
CODEN: ABPYBL; ISSN: 0065-2229
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 85 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB A special proteolipid extracted from bovine spleen capsules with CHCl3-MeOH
(2:1), separated by column chromatog. on Sephadex LH-20, and eluted between 17
and 22 ml CHCl3 bound 3H-labeled (+-)-norepinephrine [138-65-8]. The saturation curve of the binding indicated that the proteolipid contained 2
groups of sites with different dissociation consts. For 200,000 g proteolipid, 3 moles of norepinephrine were bound with high affinity and 27 moles with low affinity. Binding of **norephinephrine** to the receptor proteolipid was competitively inhibited by the α-adrenergic blocking agents, phentolamine [50-60-2] and dibenamine [51-50-3], and by the β-adrenergic blocking, agent, propranolol [525-66-6].
ACCESSION NUMBER: 1972:429507 CAPLUS
DOCUMENT NUMBER: 77:29507
TITLE: Isolation of a proteolipid from spleen capsule binding
(+-)-[3H]-norepinephrine
AUTHOR(S): Fiszer de Plazas, Sara; De Robertis, Eduardo
CORPORATE SOURCE: Fac. Med., Univ. Buenos Aires, Buenos Aires, Argent.
SOURCE: Biochimica et Biophysica Acta (1972), 266(1), 246-54
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 86 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Halothane [151-67-7], cyclopropane [75-19-4], Ethrane [13838-16-9], and diethyl ether [60-29-7] added in concns. producing a 50% decrease in the myocardial isometric contractile force of isolated guinea pig left atria did not affect either the uptake of 3H-labeled l-norepinephrine [51-41-2] or the intraneuronal monoamine oxidase [9001-66-5] activity.
ACCESSION NUMBER: 1972:413979 CAPLUS
DOCUMENT NUMBER: 77:13979
TITLE: Effects of inhalation anesthetics on the uptake and metabolism of l-3H-norepinephrine in guinea-pig atria
AUTHOR(S): Brown, Burnell R., Jr.; Tatum, Ella N.; Crout, J. Richard
CORPORATE SOURCE: Southwest. Med. Sch., Univ. Texas, Dallas, TX, USA
SOURCE: Anesthesiology (1972), 36(3), 263-7
CODEN: ANESAV; ISSN: 0003-3022
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 87 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Aggression caused by prolonged isolation of rats was accompanied by an increased content of free and a decreased content of bound norepinephrine [51-41-2] in the brain. A sedative dose of the neuroleptic, haloperidol (I) [52-86-8], (2 mg/kg) decreased the content of both free and bound fractions of norepinephrine in the brain. In animals with exptl. aggressiveness, I decreased the level of the free functionally active fraction of norepinephrine, but did not affect the bound fraction. Seduxen (diazepam) (II) [439-14-5], a tranquilizer, in the same dose decreased the content of the free fraction of norepinephrine in the brain stem of control and isolated rats.

ACCESSION NUMBER: 1972:135724 CAPLUS
DOCUMENT NUMBER: 76:135724
TITLE: Influence of neuroleptics and tranquilizers on the levels of free and bound norepinephrine fractions in the brain of rats during aggression
AUTHOR(S): Vysotskaya, N. B.; Boiko, S. S.; Aleshinkova, T. N.
CORPORATE SOURCE: Inst. Pharmacol., Moscow, USSR
SOURCE: Byulleten Eksperimental'noi Biologii i Meditsiny (1972), 73(1), 58-60
CODEN: BEBMAE; ISSN: 0365-9615
DOCUMENT TYPE: Journal
LANGUAGE: Russian

L16 ANSWER 88 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Norepinephrine-3H (I) was infused intraarterially at a constant rate of 1,

5, or 50 ng/min into the cat spleen, perfused with Krebs-bicarbonate solution

In the course of I infusion, splenic nerves were stimulated at frequencies

of 5 and 30 sec-1 for 1 min, the total norepinephrine (II), and I of the perfusate collected during stimulation, were measured; nerves were also stimulated after infusion of I. During infusion at different rates, 55% of the infused radioactivity was recovered in the venous perfusate. Of the radioactivity so recovered, .apprx.70% was due to II. Perfusing the spleen at varying flow rates (2-13 ml/min) did not appreciably affect recoveries. During stimulation at a frequency of 30 sec-1, there was a net increase in I output over the background level. In spleens perfused with either low Ca or high Mg Krebs solution, the increase in I outflow in

response to nerve stimulation during I infusion was considerably reduced, but the sp. activity of the released amine was not appreciably altered. Sp. activities of II released by nerve stimulation during infusion of I were comparable, or only slightly higher than those obtained after stopping the infusion of the amine. Retention of I during its infusion was also not significantly different in stimulated and nonstimulated portions of the same spleen. It is concluded that increase in I outflow during stimulation is probably due to enhanced release, and that nerve stimulation does not appreciably affect the uptake of infused I.

ACCESSION NUMBER: 1972:111147 CAPLUS
DOCUMENT NUMBER: 76:111147
TITLE: Effects of nerve stimulation on the uptake of **norephinephrine** by the perfused spleen of the cat
AUTHOR(S): Yamamoto, H.; Kirpekar, S. M.
CORPORATE SOURCE: Downstate Med. Cent., State Univ. New York, Brooklyn, NY, USA
SOURCE: European Journal of Pharmacology (1972), 17(1), 25-33
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 89 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Isolated rat irides from untreated rats or rats pretreated with the tyrosine hydroxylase inhibitor H44/68 or the dopamine-β-hydroxylase inhibitor FLA63 were incubated in physiol. buffer for 30 min and then superfused by buffer for 60 min in small chambers. Some of the irides were stimulated by an elec. field at 10 Hz for 60 min. Endogenous noradrenaline (NA) was enzymically determined or the irides were examined with

the fluorescence histochem. method. Irides that were not stimulated contained about 5 ng NA/iris. Stimulation reduced the NA content of irides from untreated or FLA63 pretreated rats to .apprx.60% of the unstimulated control. Stimulation caused an altered distribution of NA with a less pronounced cumulation of NA to the varicosities of the adrenergic nerve terminals. Addition of tyrosine to the superfusing buffer

did not diminish the stimulation-induced decrease of NA. In irides from rats pretreated with H44/68, stimulation reduced the NA content to .apprx.25% of the unstimulated control. A great reduction of the fluorescence intensity of the majority of the nerve terminals was observed

The difference found in stimulation-induced depletion of endogenous NA between irides of untreated and H44/68 pretreated rats is most likely due to synthesis of NA in vitro in the irides of untreated rats.

ACCESSION NUMBER: 1972:110966 CAPLUS
DOCUMENT NUMBER: 76:110966
TITLE: Synthesis of noradrenaline in isolated rat iris during

field stimulation
AUTHOR(S): Farnebo, Lars O.; Lidbrink, Peter
CORPORATE SOURCE: Dep. Histol., Karolinska Inst., Stockholm, Swed.
SOURCE: Acta Physiologica Scandinavica, Supplementum (1971), No. 371, 29-34
CODEN: APSSAD; ISSN: 0302-2994
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 90 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Bioassays for epinephrine (I) and norepinephrine(II) were done on adrenal glands from goats, sheep, cats, and rats at various stages of pregnancy and postpartum. Also, 24-hr urinary output of I and II were determined in 20

women in pregnancy, in labor, and postpartally. Results indicate that none of these 3 states produces significant changes in the I and II content of the adrenal glands. Urinary I and II output remains normal until the onset of labor when there is a marked increase in both, especially II.

Postpartally there is a gradual rise in I and II, peaking at 6-18 hr after

delivery. A case of hydatidiform mole (Destrusens) showed normal I and II

urinary output. Small amts. of both were found in the mole.

ACCESSION NUMBER: 1972:83905 CAPLUS
DOCUMENT NUMBER: 76:83905
TITLE: Epinephrine and **norephinephrine** in pregnancy. Comparative study of the adrenal gland and

catechol output in different species of animals and man
AUTHOR(S): Goodall, McC.; Diddle, A. W.
CORPORATE SOURCE: Med. Branch, Univ. Texas, Galveston, TX, USA
SOURCE: American Journal of Obstetrics and Gynecology (1971), 111(7), 896-904
CODEN: AJOGAH; ISSN: 0002-9378
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 91 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Nialamide (I) [51-12-7] pretreatment of isolated arteries produced a secondary increase in the constrictor response to extraluminal norepinephrine [51-41-2], as well as a delayed recovery from the effects of norepinephrine. Chronically denervated arteries did not display the secondary response or delayed recovery, suggesting that these actions were associated with inhibition of intraneuronal rather than extraneuronal monoamine oxidase. I treatment did not influence the effect of intraluminal norepinephrine, apparently due to the relative failure of intraluminal norepinephrine to penetrate to the sympathetic nerve terminals.

ACCESSION NUMBER: 1972:81454 CAPLUS
DOCUMENT NUMBER: 76:81454
TITLE: Relation between the roles of monoamine oxidase and sympathetic nerves in the vasoconstrictor response of the rabbit ear artery to norepinephrine
AUTHOR(S): De la Lande, I. S.; Jellett, L. B.
CORPORATE SOURCE: Dep. Hum. Physiol. Pharmacol., Univ. Adelaide, Adelaide, Australia
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1972), 180(1), 47-55
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 92 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The brain of dogs were relatively protected from anoxia caused by either decreases in inspired oxygen [7782-44-7] concentration or by sludging in the microcirculation. The administration of norepinephrine (I) [51-41-2] at 2 μg/kg moderately increased the arterial pressure with simultaneous increases in arterial, renal, and cerebral O2 pressure (pO2). Higher doses markedly increased the arterial pressure with a decrease in arterial, renal, and cerebral pO2. Thus attempts to support the circulation with I should strive for low doses with only modest increases in pressure.

ACCESSION NUMBER: 1972:54385 CAPLUS
DOCUMENT NUMBER: 76:54385
TITLE: Effect of **norephinephrine**, blood sludging, and respiratory agas change on blood and tissue oxygenation as determined with ultramicro oxygen electrodes
AUTHOR(S): Bicher, H. I.; Fitts, C. T.; Yarbrough, D. R., III
CORPORATE SOURCE: Dep. Anat., Med. Univ. South Carolina, Charleston, SC, USA
SOURCE: Surgical Forum (1971), 22, 213-15
CODEN: SUFOAX; ISSN: 0071-8041
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 93 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Norepinephrine (I) [51-41-2] stimulated glucose [50-99-7] uptake in erythrocytes and lymphocytes and inhibited it in the lymphoblast. This action was partially inhibited in the erythrocyte and was converted to inhibition in the lymphocyte by phentolamine [50-60-2]. Thus, I's effect in both is an alpha adrenergic action. The lymphoblast inhibition of glucose uptake by I was converted to stimulation by addition of propranolol [525-66-6] which indicated the I acts in this case through a beta receptor mechanism.

ACCESSION NUMBER: 1972:10464 CAPLUS
DOCUMENT NUMBER: 76:10464
TITLE: Alpha adrenergic stimulation of glucose uptake in the human erythrocyte, lymphocyte, and lymphoblast
AUTHOR(S): Hadden, J. W.; Hadden, Elba M.; Good, R. A.
CORPORATE SOURCE: Dep. Pediatr., Variety Club Heart Hosp., Minneapolis, MN, USA
SOURCE: Experimental Cell Research (1971), 68(1), 217-19
CODEN: ECREAL; ISSN: 0014-4827
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 94 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The effects of different derivs. of tyrosine (I) are considered. Reserpine given alone to rats, gave a 3-fold increase in I transaminase (II). However, rats pretreated with the monoamine oxidase inhibitor Catron showed no depletion of brain norepinephrine (III) and no significant rise in II. Incubation of II with III plus the pyridoxal 5'-phosphate (IV) cofactor inhibited III activity as much as 95%. Maximum inhibition occurred only on preincubation of III with the reaction mixture There was spectrophotometric evidence (curves shown) of complex formation between III and IV. An isosbestic point of 345 mμ indicated that the reaction can be treated in terms of a single equilibrium between IV and the product of its reaction with III. Similar effects of other complexes of amines with IV are considered, in relation to substituents on the amines. Increasing concns. of III reduced and finally abolished the induction of II by pyridoxine. A mechanism is discussed by which III may contribute to the II activity rhythm.

ACCESSION NUMBER: 1971:459335 CAPLUS
DOCUMENT NUMBER: 75:59335
TITLE: **Norephinephrine** and the circadian rhythm of rat hepatic tyrosine transaminase activity
AUTHOR(S): Black, Ira B.
CORPORATE SOURCE: Natl. Inst. Ment. Health, Bethesda, MD, USA
SOURCE: Biogenic Amines Physiol. Regul., Symp. (1970), Meeting Date 1969, 301-20. Editor(s): Blum, J. J. Prentice-Hall, Inc.: Englewood Cliffs, N. J.
CODEN: 23BPAZ
DOCUMENT TYPE: Conference
LANGUAGE: English

L16 ANSWER 95 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Rats under anaesthesia were injected with 14C-or 3H-labeled noradrenaline.
The animals were killed after 0.5-30 min and samples taken according to Ullberg (1954) for autoradiog. The results showed binding within 1 min in
the adrenal medulla and sympathetic adrenergic plexus of innervated tissues and organs. Absorption, probably from the plasma, was also demonstrated within 1 min in extraneuronal tissues, e.g. myocardial fibers. Medullary epinephrine may, by competition, diminish or limit the uptake of norepinephrine into the extraneuronal pool(s).
ACCESSION NUMBER: 1971:50202 CAPLUS
DOCUMENT NUMBER: 74:50202
TITLE: Uptake and storage of carbon-14- and tritium-labeled norepinephrine in rats
AUTHOR(S): Leder, O.; Harms, E.; Kammermeier, H.
CORPORATE SOURCE: Physiol. Inst., Univ. Freiburg/Br., Freiburg/Br., Fed.
Rep. Ger.
SOURCE: Histochemie (1970), 24(2), 130-41
CODEN: HICHAU; ISSN: 0018-2222
DOCUMENT TYPE: Journal
LANGUAGE: German

L16 ANSWER 96 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB On incubation with crude mitochondrial fractions from various areas of rabbit brain with 5-hydroxytryptamine (I), the increase in the levels of I
in the hypothalamus and corpus striatum was much higher than that in the whole brain stem; the increase in the cerebellum was quite small. Dopamine (II) and **norephinephrine** (III) reduced the level of I incorporation into the hypothalamus by 20-50%, resp., and II and III reduced incorporation into the corpus striatum by 50%. II did not alter the uptake in the cerebellum and III inhibited it only slightly. There is
evidently a considerable degree of regional specificity in the uptake of I
by I terminals since the exogenous I was mostly taken up by crude mitochondrial fractions from areas rich in endogenous I.
ACCESSION NUMBER: 1970:423025 CAPLUS
DOCUMENT NUMBER: 73:23025
TITLE: Regional specificity of 5-hydroxytryptamine uptake in rabbit brain stem
AUTHOR(S): Takatsuka, K.; Segawa, Tomio; Takagi, Hiroshi
CORPORATE SOURCE: Fac. Pharm. Sci., Kyoto Univ., Kyoto, Japan
SOURCE: Journal of Neurochemistry (1970), 17(5), 695-6
CODEN: JONRA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 97 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB N-Ethoxycarbonyl-3-morpholinosydnonimine (I) (0.10-2.0 mg/kg) given i.v. to anesthetized dogs and cats produced a gradually developing and prolonged hypotensive effect characterized by a decrease in pulse pressure
because of the greater fall in systolic than diastolic pressure. The hypotension was not antagonized by pretreatment with atropine sulfate (1 mg/kg i.v.), bilateral cervical vagotomy, spinal cord section with cervical vagotomy, or evisceration. During the hypotensive effect, the pressor response to bilateral carotid occlusion and the response of the nictitating membrane to preganglionic sympathetic stimulation were not affected, and blood pressure responses to epinephrine-HCl and **norephinephrine**-HCl were not consistently affected although I reduced the responses at the perfused vascular bed to the catechol amines but not to angiotensin II given directly into the perfusion circuit. These results suggested that I did not produce its hypotensive effect through central, sympathetic, and parasympathetic nervous systems or a specific blockade of the α-adrenergic receptive system. The rates of blood flow in the femoral and coronary arteries of dogs were not increased by intraarterial injections of I, and the decreased in parallel with the hypotension induced by i.v. injection of the drug. In constant flow perfusion expts., the perfusion pressure of the femoral artery was not reduced in parallel with I-induced hypotension. These results indicate that I-induced hypotension resulted not from a dilator action of peripheral resistance vessels but rather from a decreased cardiac output by either a decreased venous return or by a depressed cardiac function. The drug did not affect isolated atria, ventricular strip, and ileum in a concentration from 1 to 100 μg/ml. I was active orally as sublingually in
anesthetized dogs.
ACCESSION NUMBER: 1970:402430 CAPLUS
DOCUMENT NUMBER: 73:2430
TITLE: Hypotensive action of N-ethoxycarbonyl-3-morpholinosydnonimine, SIN-10
AUTHOR(S): Kikuchi, Kenzo; Hirata, Minoru; Nagaoka, Akinobu
CORPORATE SOURCE: Biol. Res. Lab., Takeda Chem. Ind., Ltd., Osaka, Japan
SOURCE: Japanese Journal of Pharmacology (1970), 20(1), 102-15
CODEN: JJPAAZ; ISSN: 0021-5198
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 98 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The effects of L-noradrenaline (1-4 μg/kg i.v.), Na pentobarbital (4-6 mg/kg) and adrenolitico (1,6-dimethyl-8β-(5-bromonicotinoyloxymethyl)met hoxyergoline) (50-299 μg/kg) on the cerebral blood flow, the cortical pH, pCO2, and pO2, the end-expiratory CO2 concentration, and on the arterial pressure were studied in cats. During
artificial respiration noradrenaline increased cerebral blood flow, pH, pO2, and arterial pressure, reduced pCO2, and did not affect end-expiratory CO2 levels within 1 min; similar results were produced during spontaneous respiration except that pH was decreased and pCO2 was increased. Within 15 min, pentobarbital decreased cerebral blood flow, pCO2, pO2, arterial pressure, and end-expiratory CO2 and increased pH during artificial respiration; during spontaneous respiration, pH was decreased, pCO2 and end-expiratory CO2 increased, and the decrease in blood flow was less by a factor of 9 and the pO2 and arterial pressure were 6 and 2.5 times more than during artificial respiration. One min after the adrenolitico injection in artificially respiring cats, blood flow, pH, pO2, and arterial pressure were reduced and pCO2 was increased; during spontaneous respiration, the decreases in blood flow and pH were greater but the effects on the other parameters were of lesser magnitude than during artificial respiration. Acidification of the cerebral cortex increased cerebral blood flow and reduced cerebral vascular resistance, while alkalinization produced the opposite effects. The reactions of cerebral vascular resistance during the action of different vasoactive agents are modified by simultaneous influences on the H+ concns. in the vascular walls of the resistance vessels. The variation in H+ concns. are
not only caused by local metabolic changes linked to functional cortical changes but also by variations in the transport of substances through vascular walls and by variations in ventilation. Since blood pressure and
cortical vascular resistance are interacting with acid-base variations of the cortex, the organism can compensate extreme variations of 1 of these factors by variation of other factors in this mes hed regulatory system.
ACCESSION NUMBER: 1970:129069 CAPLUS
DOCUMENT NUMBER: 72:129069
TITLE: Regulation of local cortical cerebral blood flow following injections of norepinephrine, pentobarbital,
and adrenolitico
AUTHOR(S): Bienmueller, Heinrich; Betz, Eberhard
CORPORATE SOURCE: Physiol. Inst., Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.
SOURCE: Aerztliche Forschung (1970), 24(4), 97-111
CODEN: ARZFAN; ISSN: 0001-9496
DOCUMENT TYPE: Journal
LANGUAGE: German

L16 ANSWER 99 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Using a sinus node-interventricular septum perfusion technique, the effects of norepinephrine (5.0 μg/kg, intraarterially), isoproterenol (6.5, or 0.75 μg/kg, intraarterially), and sympathetic nerve stimulation upon the myocardium, and the effect of α-adrenergic blockade with verapamil (18 μg/kg, intraarterially, infused for 2-3 min) upon these responses were studied in dogs. Norepinephrine and sympathetic nerve stimulation increased the heart rate of these animals with outbursts of arrhythmias and atrial fibrillation, whereas isoproterenol induced similar increases in the heart rate, but caused no arrhythmias. Pretreatment of dogs with verapamil inhibited both sympathetic nerve stimulation and norepinephrine-induced arrhythmias, enhanced the tachycardia, and increased the contractile force produced by all 3 procedures. The observed responses to sympathetic nerve stimulation, **norephinephrine**, and isoproterenol, and their modification by verapamil, may be localized myocardial responses involving both cardiac α- and β-adrenergic mechanisms.
ACCESSION NUMBER: 1970:98857 CAPLUS
DOCUMENT NUMBER: 72:98857
TITLE: Adrenergic mechanisms in the initiation of cardiac arrhythmias
AUTHOR(S): Garvey, H. Lloyd
CORPORATE SOURCE: Fac. Med., Univ. Ottawa, Ottawa, ON, Can.
SOURCE: Archives Internationales de Pharmacodynamie et de Therapie (1969), 182(2), 376-90
CODEN: AIPTAK; ISSN: 0003-9780
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 100 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Tyrosine hydroxylase was partially purified from the human pheochromocytoma. Properties of the pheochromocytoma enzyme were similar to those of the bovine adrenal enzyme. The enzyme required tetrahydropteridine as a cofactor and was markedly activated by Fe2+. Tyrosine hydroxylase isolated from the human pheochromocytoma was less sensitive to the inhibition by norepinephrine than the enzyme from the bovine adrenal medulla, either in the presence or absence of Fe2+. It is suggested that the uncontrolled excessive production of norepinephrine in the pheochromocytoma could be partly due to altered sensitivity of tyrosine hydroxylase to norepinephrine inhibition.
ACCESSION NUMBER: 1970:96844 CAPLUS
DOCUMENT NUMBER: 72:96844
TITLE: Partial separation and properties of tyrosine hydroxylase from the human phenochromocytoma: effect of norepinephrine
AUTHOR(S): Nagatsu, Toshiharu; Yamamoto, Tomiko; Nagatsu, Ikuko
CORPORATE SOURCE: Sch. Dent., Aichi-Gakuin Univ., Nagoya, Japan
SOURCE: Biochimica et Biophysica Acta (1970), 198(2), 210-18
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 101 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Effects of tyramine (0.5 mg/kg, i.v.), ephedrine (1.0 mg/kg, i.v.), and amphetamine (1.0 mg/kg, i.v.) on arterial blood pressure were studied in dogs with or without pretreatment with nialamide (20 mg/kg, i.p.). The hypertensive effect of tyramine was unaltered by ephedrine and amphetamine, although there was a crossed tachyphylaxis between the α-methylated amines in dogs that were not treated with nialamide. Pretreatment with nialamide increased the pressor effect of tyramine and the crossed tachyphylaxis between tyramine and α-methylated amines. This effect was due to the prolonged occupation of intraneuronal storage sites by tyramine.
ACCESSION NUMBER: 1970:88738 CAPLUS
DOCUMENT NUMBER: 72:88738
TITLE: Crossed tachyphylaxis between tyramine and some alpha methylated sympathomimetic amines
AUTHOR(S): De Moraes, Sergio; Varela de Carvalho, F.; Aragao, J. A.
CORPORATE SOURCE: Fac. Vet Med., Univ. Sao Paulo, Sao Paulo, Brazil
SOURCE: Pharmacology (1970), 3(3), 168-76
CODEN: PHMGBN; ISSN: 0031-7012
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 102 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Catecholaminergic neurons, which take up and retain exogenous norepinephrine-3H, were studied, by means of high-resolution radioautography, in the substantia nigra, the substantia grisea periventricularis, and the locus ceruleus of the rat. Glutaraldehyde was the most suitable fixative for preserving the labeled amine in situ; norepinephrine-3H itself, rather than metabolites, accounted for most of the reactions detected in catecholaminergic neurons. At various time intervals after an intraventricular injection of norepinephrine-3H, the tracer reached a concentration 15-100 times higher, and disappeared at a slower rate, in presynaptic axons (t1/2 = 4 hr) than in nerve cell bodies (t1/2 = 0.8-1.3 hr). After pretreatment with a monoamine oxidase inhibitor, the radioautographic reactions increased and persisted longer, especially in the preterminal axons. Within neurons, the labeled amine was ubiquitously distributed in the nerve cell body and concentrated in presynaptic axons and synaptic terminals of various morphol. types. Although large granular vesicles were usually present in the labeled axonal bulbs, no structural characteristic could be specifically ascribed to catecholaminergic neurons. Exogenous norepinephrine bound to macromol. complexes is seeminglypresent in all parts of catecholaminergic neurons and mainly concd.within presynaptic axons.
ACCESSION NUMBER: 1970:86726 CAPLUS
DOCUMENT NUMBER: 72:86726
TITLE: Intraneural distribution of exogenous norepinephrine in the central nervous system of the rat
AUTHOR(S): Descarries, Laurent; Droz, Bernard
CORPORATE SOURCE: Dep. Biol., C.E.A., Saclay, Fr.
SOURCE: Journal of Cell Biology (1970), 44(2), 385-99
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 103 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The relations between blood flow in epigastric adipose tissue and free fatty acid (FFA) release were studied in rabbits. The close intraarterial infusion of the fat mobilizers, Synacthen, β-MSH, luteotropin, growth hormones, and glucagon, increased blood flow and released FFA into the venous effluent; both fat mobilization and vasodilatation continued for about an hr after termination of infusions. Infusion of **norephinephrine**, which does not release FFA in rabbitepigastric fat tissue, evoked vasoconstriction. No vasodilator substance was detected in the venous effluent from the activated adipose tissue, but a vasodilator was present in acid-ether exts. of adipose tissue excised during a period of fat mobilization. This suggested that a vasodilator substance is released or formed inadipose tissue during fat mobilization.

ACCESSION NUMBER: 1970:75211 CAPLUS
DOCUMENT NUMBER: 72:75211
TITLE: Mechanism of functional vasodilatation in rabbit epigastric adipose tissue
AUTHOR(S): Lewis, Graham Pritchard; Matthews, John
CORPORATE SOURCE: CIBA Lab., Horsham, UK
SOURCE: Journal of Physiology (Cambridge, United Kingdom) (1970), 207, 15-30
CODEN: JPHYA7; ISSN: 0022-3751
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 104 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Epididymal fat pads of rats treated with lysine vasopressin (100 milliunits/100 g) released significantly less free fatty acids and glycerol than the tissue of control rats. Lysine vasopressin treatment effectively blocked the stimulatory effect of norepinephrine (200 μg/100 g s.c.) on adipose tissue lipolysis. Lysine vasopressin (40 mU/100 g s.c.), when given in vivo, was a potent inhibitor of hormone-sensitive lipase activity in white adipose tissue. On the other hand, appreciable change was not observed in the lipase activity of brown adipose tissue following lysine vasopressin treatment. Lipoprotein lipase activity of epididymal white fat as well as interscapular brown fat was not affected by either lysine vasopressin or norepinephrine injections.

ACCESSION NUMBER: 1970:51437 CAPLUS
DOCUMENT NUMBER: 72:51437
TITLE: Inhibition of adipose tissue lipase activity following administration of vasopressin
AUTHOR(S): Moriya, Kiyoshi; Itoh, Shinji
CORPORATE SOURCE: Sch. Med., Hokkaido Univ., Sapporo, Japan
SOURCE: Japanese Journal of Physiology (1969), 19(6), 834-40
CODEN: JJPHAM; ISSN: 0021-521X
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 105 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Abolition of the circadian rise of plasma 17-hydroxy corticosteroid levels in the cat was produced by types of drugs that alter serotonin levels or action: (1) 3-(2-aminobutyl)indole acetate, which elevates central nervous system serotonin levels; (2) p-chloroamphetamine, which depletes central nervous system serotonin levels; (3) 2'-[[3-(dimethylamino)propyl]thio]cinnamanilide, which acts as a competitive inhibitor of serotonin at the receptor site; and (4) cyproheptadine, which is a serotonin antagonist. L-α-Methyl-p-tyrosine, which lowers central nervous system **norephinephrine** levels, and reserpine, which lowers both central nervous system serotonin and norepinephrine levels, do not block the circadian rise of plasma 17-hydroxy corticosteroid levels. None of the agents abolishing the circadian rise block: (1) the adrenal response to adrenocorticotrophic hormone; (2) the pituitary-adrenal response to lysine vasopressin; (3) the hypothalamic-pituitary-adrenal response to either insulin hypoglycemia or Pseudomonas polysaccharide administration. Central nervous system mechanisms and (or) structures involved in the regulation of circadian periodicity of adrenal steroid levels are probably different from those mediating stress-initiated adrenal cortical responses.

ACCESSION NUMBER: 1970:40673 CAPLUS
DOCUMENT NUMBER: 72:40673
TITLE: Serotonin mediation of circadian periodicity of plasma 17-hydroxycorticosteroids
AUTHOR(S): Krieger, Dorothy T.; Rizzo, Frank
CORPORATE SOURCE: Mt. Sinai Sch. of Med., New York, NY, USA
SOURCE: American Journal of Physiology (1969), 217(6), 1703-7
CODEN: AJPHAP; ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 106 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The uptake of norepinephrine by rabbit platelets at pH 6.0 was increased by Na+ and to a lesser extent by K+. In contrast, the retention of norepinephrine by the platelets was impaired to a greater extent by a lack of K+ than by a lack of Na+. At high levels, K+ inhibited norepinephrine uptake, whereas Na+ continued to stimulate norepinephrine uptake over a wide range of concns. The uptake of tryptamine by the platelets was not influenced by changes in the levels of Na+ and K+ in the incubation medium. Ouabain inhibited the K+- but not the Na+-dependent component of norepinephrine uptake. Chlorpromazine and impramine inhibited both the Na+ and the K+-dependent uptake of norepinephrine, whereas propranolol and phenoxybenzamine inhibited norepinephrine uptake by the inhibition of a process not dependent on either Na+ or K+.

ACCESSION NUMBER: 1969:459320 CAPLUS
DOCUMENT NUMBER: 71:59320
TITLE: Effects of sodium and potassium on **norephinephrine** uptake by rabbit platelets and the inhibition of this process by drugs
AUTHOR(S): McLean, J. R.; Potoczak, Doris
CORPORATE SOURCE: Res. Lab., Parke, Davis and Co., Ann Arbor, MI, USA
SOURCE: Archives of Biochemistry and Biophysics (1969), 132(2), 416-22
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 107 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Chicks (1-5-days-old) were made hyperactive and aggressive by an injection
of 15 mg. imipramine-HCl/kg. Injection of 5-20 micromoles norepinephrine-HCl/kg. 90 min. after treatment with imipramine-HCl produced behavioral depression in the chick in a monotonic, dose-response manner and antagonized the behavioral effects of imipramine-HCl. Associated
with this behavioral antagonism was a relative decrease in the radioactivity in brain normetanephrine and 3-methoxy-4-hydroxymandelic acid when isotopic norepinephrine-HCl was infused following imipramine-HCl pretreatment. Thus, imipramine may block the excess of norepinephrine to the postsynaptic membrane as well as interfering with other aspects of norepinephrine inter- and intracellular mobility.

ACCESSION NUMBER: 1969:429111 CAPLUS
DOCUMENT NUMBER: 71:29111
TITLE: Imipramine antagonism of the CNS (central nervous system) effects of **norephinephrine** behavioral and biochemical correlates
AUTHOR(S): Mandell, Arnold J.; Spooner, Charles E.; Winters, Wallace D.; Cruikshank, M.; Sabbot, I. M.
CORPORATE SOURCE: Brain Res. Inst., Los Angeles, CA, USA
SOURCE: International Journal of Neuropharmacology (1969), 8(3), 235-44
CODEN: IJNEAQ; ISSN: 0375-9458
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 108 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB There is rapid accumulation of gangliosides (I) with age in mouse, rat, and human brain tissue. This is followed by an accumulation of cerebrosides (II). II and sphingomyelin occur in the myelin sheath; I occurs elsewhere. These lipids are those which provide structural integrity where this integrity must be maintained for a long period of time. A portion of the sphingosine mol. contains a hydroxyl group and an amino group. Its structure is markedly similar to the structure of monoglyceride. Both acetylcholine (III) and I concentrate in the nerve terminal
fraction. Subfractionation of the osmotically disrupted nerve terminal fraction into "ghosts" and an enriched synaptic vesicle fraction showed that I is found primarily in the synaptic vesicle fraction which also contains III. The lipids bind III. The vesicle fractions from the brain were relatively nonspecific. They bound III, choline, **norephinephrine**, serotonin, and γ-aminobutyric acid. This binding, even in the vesicles, was due primarily to the phospholipids, which are spatially oriented and spaced by the cholesterol present. This permits maximum binding of the neurohormones. The nerve terminal fraction
binding is probably specific. Active transport may be involved. The binding is not inhibited by K+ and the bound III is osmotically sensitive.

ACCESSION NUMBER: 1969:1516 CAPLUS
DOCUMENT NUMBER: 70:1516
TITLE: Lipids and neuronal development
AUTHOR(S): Burton, Robert M.
CORPORATE SOURCE: Sch. of Med., Washington Univ., St. Louis, MO, USA
SOURCE: United States, Public Health Service Publication (1967), No. 1791, 60-75
CODEN: XPHPAW; ISSN: 0500-3148
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 109 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB DL-α-Methyltyrosine was injected i.p. into mice in a dose of 80 mg./kg. The mice, which had been previously made aggressive by maintenance in isolation cages, were kept, after treatment, either in isolation, in bisexual pairs, or in groups of 8. Total brain levels of **norephinephrine** and dopamine were no lower in fighting or grouped mice than in nonstimulated controls, although after 2.5 hrs. the norepinephrine levels were lower in the brain stem and higher in the telencephalon of the fighting mice than in their undisturbed controls. The average dopamine level was slightly higher in stimulated mice in each experiment Stimulus-induced conservation of brain catechol amines may have
compensated for the increased demand for catechol amine release under these conditions. 17 references.

ACCESSION NUMBER: 1968:457836 CAPLUS
DOCUMENT NUMBER: 69:57836
TITLE: Failure of natural stimuli to accelerate brain catechol amine depletion after biosynthesis inhibition
with α-methyltyrosine
AUTHOR(S): Welch, Annemarie S.; Welch, Bruce L.
CORPORATE SOURCE: Mem. Res. Center and Hosp., Knoxville, TN, USA
SOURCE: Brain Research (1968), 9(2), 402-5
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 110 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Metabolic energy of the brain appears to have a crude relationship to consciousness. Exceptions include such conditions as schizophrenia and the psychosis resulting from LSD. During normal sleep O consumption by the brain is not altered, as in coma or anethesia. Although the mechanism
may be obscure, interference with protein synthesis does block the ability
to consolidate memory patterns. The disorder of thought processes as in schizophrenia may be the result of an abnormal metabolism of epinephrine into hallucinogenic agents. The mood-altering drugs may act being antagonistic to amines found in the brain. Both these drugs and electroconvulsive shock increased the amount of **norephinephrine** in the brain of rats.

ACCESSION NUMBER: 1968:434193 CAPLUS
DOCUMENT NUMBER: 69:34193
TITLE: Biochemistry and mental states
AUTHOR(S): Kety, Seymour S.
CORPORATE SOURCE: Harvard Med. Sch., Boston, MA, USA
SOURCE: California Medicine (1968), 108(5), 362-8
CODEN: CAMEAS; ISSN: 0008-1264
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 111 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB In cats, the response of the blood pressure to norepinephrine was enhanced by imipramine, desipramine, atropine, and the antihistaminics, tripelennamine, thenyldiamine, carbinoxamine, and chlorpheniramine and was reduced by promazine. The **norephinephrine**-induced contraction of the nictitating membrane was potentiated significantly by desipramine and to a lesser extent by imipramine, tripelennamine, and thenyldiamine, but not by atropine or the other 2 antihistaminics. Hypothermia induced in mice by 2 mg. of reserpine/kg. i.p. was reduced by imipramine, desipramine, amitriptyline, promazine, atropine, and the 4 antithistaminics. Other antihistamines, including thonzylamine, Antergan, and dimethindene, were inactive. The stimulant effects of dopa in pargyline-pretreated mice was enhanced by the tricyclic antidepressants, atropine, methylatropine, tripelennamine, and particularly chlorpheniramine. Chlorpromazine consistently reduced dopa-induced motor hyperactivity. None of the 4 pharmacol. test for non-monoamine oxidase inhibiting antidepressants is specific in that, dependent on the procedure utilized, certain antihistaminics and anticholinergics are active. Only imipramine and desipramine were shown pos. in all 4 procedures.
ACCESSION NUMBER: 1968:417911 CAPLUS
DOCUMENT NUMBER: 69:17911
TITLE: Effect of imipramine on central adrenergic mechanisms
AUTHOR(S): Sigg, E. B.; Hill, R. T.
CORPORATE SOURCE: Geigy Res. Div., Geigy Chem. Corp., Ardsley, NY, USA
SOURCE: Neuro-Psycho-Pharmacol., Proc. Int. Congr. Coll. Int. Neuro-Psycho-Pharmacol., 5th, Washington, D. C. (1967), Volume Date 1966 367-72
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 112 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Tricyclic antidepressants modify the fate of **norephinephrine** (I) released by reserpine from intraneuronal storage sites in rats in vivo. The change in the metabolic fate of the released I is the biochem. basis for the shift in autonomic and behavioral activity which occurs when reserpine-like drugs are administered after tricyclic antidepressants.
ACCESSION NUMBER: 1968:401603 CAPLUS
DOCUMENT NUMBER: 69:1603
TITLE: Adrenergic mechanisms in the central action of tricyclic antidepressants and substituted phenothiazines
AUTHOR(S): Sulser, F.; Dingell, J. V.
CORPORATE SOURCE: Sch. of Med., Vanderbilt Univ., Nashville, TN, USA
SOURCE: Agressologie (1968), 9(2), 281-7
CODEN: AGSOA6; ISSN: 0002-1148
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 113 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Exogenous K+ potentiated cold (4°) contraction in isolated rat intestine but had no similar effect on guinea pig intestine. Protriptyline, which by itself slightly relaxed the rat vas deferens, greatly potentiated the contractions induced by cold stimulus, K+, and norepinephrine. **Norephinephrine** contraction was not modified by cold stimulation or K+. Reserpine was species-specific on the isolated intestine: it abolished cold contraction in guinea pigs, while in rats only the spontaneous movements were decreased. However, the cold response of the intestine in both species was inhibited by in vivo reserpinization. Cooling guinea pig intestine in the presence of reserpine increased K+ release, a mechanism which may be responsible for some of reserpine's toxic action on contracting organs, such as cardiac insufficiency in rats accompanied by K+ release and in patients treated with cardiac glycosides and reserpine.
ACCESSION NUMBER: 1968:103659 CAPLUS
DOCUMENT NUMBER: 68:103659
TITLE: Cold stimulation of organs in relation to potassium concentration and drug action
AUTHOR(S): Arbona I., Juan
CORPORATE SOURCE: Esc. Med. "Jose Vargas", Univ. Cent. Venezuela, Caracas, Venez.
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1968), 127(2), 359-63
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 114 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Addition of caffeine to pig feed, in doses of 1.5 g./kg. of feed during 4 weeks, increased N retention by 7.9% in 65 kg. pigs fed 2 kg. of feed per day. Feeding weanling pigs the same dose of caffeine for several months did not significantly affect feed efficiency, growth rate, and protein content of the carcass, but reduced depth of fat deposition by 6.6-13.1%, as compared with control animals. When given in 3 g./kg. of feed doses, caffeine restricted feed consumption and caused a skin rash. In comparison with control animals, injection of norepinephrine (2 mg./kg., i.m.) into pigs treated with 14C-labeled palmitate increased the level of expired 14C-labeled O2 up to 10 times and caffeine (50 mg./kg.) treatment increased it up to 6 times, whereas treatment with colchicine (0.1 mg./kg.) had no effect on it. Norepinephrine produced a large increase in the plasma levels of free fatty acids, whereas caffeine produced a moderate increase and colchicine only a slight increase in these levels. Thus, caffeine is capable of mobilizing body fat and, under restricted feeding conditions, of increasing growth rate and feed efficiency in growing pigs. 18 references.
ACCESSION NUMBER: 1968:103064 CAPLUS
DOCUMENT NUMBER: 68:103064
TITLE: Effect of caffeine on nitrogen retention, carcass composition, fat mobilization, and the oxidation of 14C-labeled body fat in pigs
AUTHOR(S): Cunningham, Hugh M.
CORPORATE SOURCE: Canada Dep. Agr., Nappan, NS, Can.
SOURCE: Journal of Animal Science (Savoy, IL, United States) (1968), 27(2), 424-30
CODEN: JANSAG; ISSN: 0021-8812
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 115 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Atria with attached functional sympathetic postganglionic fibers were isolated from rabbits and placed in modified Ringer's solution at 30°. Transmembrane potentials were recorded from pacemaker fibers of the sinoatrial node. Typical effects of sympathetic nerve stimulation were an increase in the slope of slow depolarization during diastole and an acceleration of the pacemaker rate. In .apprx.25% of the pacemaker fibers studied, nerve stimulation did not induce the increase in the slope in spite of marked acceleration of pacemaker rate. The 90% duration was decreased and the depolarization time was prolonged after the stimulation.
Similar changes in membrane potentials were induced by the application of **norephinephrine**. However, the incidence of pacemaker shift was observed more in the presence of norepinephrine than in response to sympathetic stimulation. When the threshold potential was lowered because of the conversion of the true pacemaker fiber to a latent pacemaker fiber, the size of the overshoot was not increased. Similar changes in the action potential duration and the depolarization time in response to sympathetic stimulation and norepinephrine application were elicited when the sinoatrial node was driven at interstimulus intervals of <370 msec. Cardiac norepinephrine might not induce changes in membrane potential during systole but during diastole.

ACCESSION NUMBER: 1968:47603 CAPLUS
DOCUMENT NUMBER: 68:47603
TITLE: Influence of sympathetic stimulation on transmembrane potentials in the sinoatrial node
AUTHOR(S): Toda, Noboru; Shimamoto, Kiro
CORPORATE SOURCE: Fac. Med., Kyoto Univ., Kyoto, Japan
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1968), 159(2), 298-305
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 116 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Replacement of 30% of the NaCl content of the modified Krebs-Ringer solution by sucrose to maintain osmolarity had no effect on the frequency of the isolated rabbit auricle but did increase the strength of contraction. Norepinephrine and tyramine showed their normal effects of increasing rate, but did not increase the strength of contraction beyond that due to the low Na content of the medium. Angiotensin did not affect the rate of contraction.

ACCESSION NUMBER: 1967:440600 CAPLUS
DOCUMENT NUMBER: 67:40600
TITLE: Influence of sodium reduction in the medium on the **norephinephrine**, tyramine, and angiotensin effects upon the isolated rabbit atria
AUTHOR(S): Illanes, Alejandro; Ortiz, Aurelio; Perez-Olea, Jaime
CORPORATE SOURCE: Univ. Chile, Santiago, Chile
SOURCE: Archivos de Biologia y Medicina Experimentales (1966), 3(2-3), 130-5
CODEN: ABMXA2; ISSN: 0004-0533
DOCUMENT TYPE: Journal
LANGUAGE: Spanish

L16 ANSWER 117 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Rat, rabbit, or bovine phenethanolamine N-methyltransferase, which catalyzes the N-methylation of l-**norephinephrine** in the final step of epinephrine biosynthesis, was inhibited in vitro by added epinephrine (100 μM), which sharply reduced velocity without affecting the Km for the substrate. The enzyme might be suppressed in the normal adrenal gland by the presence of high levels of epinephrine. Increased secretion of epinephrine would decrease the amount of product inhibition, resulting in increased methylation of l-**norephinephrine**.

ACCESSION NUMBER: 1967:408175 CAPLUS
DOCUMENT NUMBER: 67:8175
TITLE: Inhibition of phenethanolamine N-methyltransferase by its product, epinephrine
AUTHOR(S): Fuller, Ray W.; Hunt, Joseph M.
CORPORATE SOURCE: Eli Lilly and Co., Indianapolis, IN, USA
SOURCE: Life Sciences (1967), 6(10), 1107-12
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 118 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Unavailable

ACCESSION NUMBER: 1967:400296 CAPLUS
DOCUMENT NUMBER: 67:296
TITLE: Studies of the enzymes involved in the biosynthesis of **norephinephrine**
AUTHOR(S): Levitt, Morton
CORPORATE SOURCE: Howard Univ., Washington, DC, USA
SOURCE: (1967) 147 pp. Avail.: 66-12,471
From: Diss. Abstr. B 1967, 27(7), 2462-3
DOCUMENT TYPE: Dissertation
LANGUAGE: English

L16 ANSWER 119 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB cf. preceding abstract. The Easson-Stedman hypothesis that dextro isomers of sympathomimetic amines have pharmacol. activities similar to their corresponding deoxy derivs. was tested in the catechol amine-depleted (reserpine, 5 mg./kg., i.p., 16-24 hrs. previously) rat vas deferens. Cumulative dose-response curves were obtained, in vitro, for D-and L-isomers of norepinephrine, epinephrine, cobefrin, metaraminol, phenylephrine, synephrine, octopamine, norephedrine, and ephedrine and their corresponding deoxy derivs., dopamine, epinine, α-methyldopamine, α-methyl m-tyramine, m-tyramine, N-methyltyramine, tyramine, (+)-amphetamine, and (+)- methamphetamine, resp. All D(-) isomers retained their ability to produce a contraction and were more active than their L(+) isomers or deoxy derives. L(+)-Norepinephrine and L(+)-epinephrine are essentially directly-acting and their effects were equal to those of dopamine and epinine, resp. All other L(+) isomers posses a considerable indirect component, as do their deoxy derivs., and both groups produced essentially similar effects. The results suggest that the Easson-Stedman hypothesis holds true over a wide range of substances in the catechol amine-depleted preparation but not in the untreated preparation where the dose-response curves of indirectly-acting deoxy derivs. and L(+) isomers appear to be related to their known affinity for catechol amine uptake sites. Further classification of sympathomimetic amines is carried out.

ACCESSION NUMBER: 1967:35097 CAPLUS
DOCUMENT NUMBER: 66:35097
TITLE: Steric aspects of adrenergic drugs. II. Effects of DL-isomers and deoxy derivatives on the reserpine-pretreated vas deferens
AUTHOR(S): Patil, Popat N.; LaPidus, Jules B.; Campbell, Duncan; Tye, Arthur
CORPORATE SOURCE: Ohio State Univ., Columbus, OH, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1967), 155(1), 13-23
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 120 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The action of D and L isomers of **norephinephrine**, epinephrine, cobefrin, metaraminol, phenylephrine, octopamine, synephrine, noreph. edrine, ephedrine, and pseudo ephedrine and their deoxy derivs. on the isolated rat vas deferens was studied in the light of the Easson-Stedman hypothesis that dextro isomers act like deoxy derivs. The dose-response curves and median effective dose values of l(+)-norepinephrine and L(+)-epinephrine were indeed essentially the same as those of their deoxy derivs., dopamine and epinine, resp. In all other cases, dextro isomers produced much less contraction of the vas deferens than their deoxy derivs. This indicates that in the normal vas deferens the hypothesis holds true for directly-acting L(+) isomers and their deoxy derivs., but not for indirectly-acting compds. In the latter case, dose-response curves appear to be related to the affinity of these compds. for catechol amine uptake sites. The importance of the relative configurations of the β-hydroxy l and α-Me groups in relation to sympathomimetic effect is discussed.

ACCESSION NUMBER: 1967:35096 CAPLUS
DOCUMENT NUMBER: 66:35096
TITLE: Steric aspects of adrenergic drugs. I. Comparative effects of DL isomers and deoxy derivatives
AUTHOR(S): Patil, Popat N.; LaPidus, Jules B.; Tye, Arthur
CORPORATE SOURCE: Ohio State Univ., Columbus, OH, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1967), 155(1), 1-12
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 121 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Levels of brain amines were determined in 3 strains of chicks from hatching to 8 weeks of age, i.e., broiler strain (males), White Leghorn strain (females), and a crossbred strain of Rhode Island Reds and Barred Plymouth Rock (males). The effect of feeding excess dietary L-phenylalanine (I) on brain amines was also studied in chicks. Norephinephine (II) and serotonin (III) levels increased in growing chicks of the broiler strain. After the lst week of age, however, concns. of both amines showed no further increases. There was no difference in the III content among the 3 strains when compared at 4 weeks of age. However, the II content in the broiler strain was appreciably higher than those of the other strains. Feeding I had no effect on either II or dopamine level in the brain, although there was a difference in the normal level of II among the 3 strains. In the broiler strain, feeding 5% I decreased the brain III content. In the other strains, however, slight increases in III levels occurred after feeding 2 and 4% I but not at the 8%. There was no effect on brain III levels when the broiler strain was fed a basal diet for 4 weeks and then changed to a diet containing 5% I for 4 weeks, although these animals lost .apprx.33% of their initial weight at 4 weeks of age. In contrast, the chicks previously fed a 5% I diet for 4 weeks and then changed to basal diet for 4 weeks gained weight rapidly and had normal or higher brain III levels.

ACCESSION NUMBER: 1967:17393 CAPLUS
DOCUMENT NUMBER: 66:17393
TITLE: Brain amines and brain weights in growing chicks. Some normal values and effects of feeding excess dietary L-phenylalanine
AUTHOR(S): Pscheidt, Gordon R.; Tamimie, Hakki S.
CORPORATE SOURCE: Galesburg State Res. Hosp., Galesburg, IL, USA
SOURCE: Biochemical Pharmacology (1966), 15(10), 1629-32
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 122 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The turnover rates of norepinephrine were measured in rat cerebellum, hypothalamus, medulla oblongata, striatum, midbrain, hippocampus, and cerebral cortex after the animals had been given intraperitoneal injections of 200 mg. of L-α-methyl-p-tyrosine/kg., intraventricular injections of 1.5 γ of labeled dopamine, or after intraventricular injections of 0.15 γ of labeled DL-norepinephrine. The rate of formation of norepinephrine/g. of tissue was greater in the hypothalamus although the turnover rate is greater in the cerebellum. The 3 exptl. procedures indicated that the disposition of norepinephrine after intraventricular injections of labeled DL-**norephinephrine** represented metabolism of endogenous stores of norepinephrine in the brain.

ACCESSION NUMBER: 1966:432878 CAPLUS
DOCUMENT NUMBER: 65:32878
ORIGINAL REFERENCE NO.: 65:6140e-f
TITLE: Regional differences in the rate of turnover of norepinephrine in the rat brain
AUTHOR(S): Iversen, L. L.; Glowinski, J.
CORPORATE SOURCE: Lab. Clin. Sci., Natl. Inst. of Mental Health, Bethesda, MD
SOURCE: Nature (London, United Kingdom) (1966), 210(5040), 1006-8
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 123 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB The response of the renal vaseulature to various intraarterially administered drugs was determined in rats with nephrotoxic serum nephrosis and aminonucleoside nephrosis. **Norephinephrine**, angiotensin, and vasopressin caused large increases in kidney perfusion pressure and (up to 100 mm.), in both nephrotic groups and their resp. controls. The renal vascular resistance was unaffected by the disease.
ACCESSION NUMBER: 1966:53562 CAPLUS
DOCUMENT NUMBER: 64:53562
ORIGINAL REFERENCE NO.: 64:10055b-c
TITLE: Renal vascular responses to drugs in experimental nephrosis in rats
AUTHOR(S): Rosenthale, Marvin E.; Baum, Thomas
CORPORATE SOURCE: Pharmacol.Evaluation Sect., Wyeth Labs., Inc., Radnor, PA
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1965), 120(3), 689-92
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 124 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Antiserum injected into newborn rats for 6 or 7 days had decreased the number of cells in the superior cervical and stellate ganglia 87 and 81%, resp., when the animals were examined 2-10 months after treatment, and it also had decreased the action potentials of the adrenergic ganglia 87%. Administration of 10 mg. of the monoamine oxidase inhibitor, Catron (JB-516),/kg. increased the adrenergic content of norepinephrine in normal rats and slightly increased the content of norepinephrine in the superior cervical and stellate ganglia from antiserum-treated rats, indicating that the surviving cells in antiserum-treated rats can synthesize norepinephrine.
ACCESSION NUMBER: 1966:30066 CAPLUS
DOCUMENT NUMBER: 64:30066
ORIGINAL REFERENCE NO.: 64:5604a-b
TITLE: Effects of immunosympathectomy on the superior cervical ganglion and other adrenergic tissues of the rat
AUTHOR(S): Klingman, Gerda I.; Klingman, Jack D.
CORPORATE SOURCE: State Univ. of New York, Buffalo
SOURCE: Life Sciences (1965), 4(22), 2171-9
CODEN: LIFSAK; ISSN: 0024-3205
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 125 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Staining of animal brain tissues with Geigy Blue (C.I. Direct Blue 53) revealed penetration of intra-arterially injected heparin, ascorbic acid, reserpine, orphenadrine, **norephinephrine**, and serotonin.
ACCESSION NUMBER: 1966:14073 CAPLUS
DOCUMENT NUMBER: 64:14073
ORIGINAL REFERENCE NO.: 64:2615g-h
TITLE: Effect of modern (psychotropic and anticoagulant) drugs on permeability--modes of action on the blood-brain barrier
AUTHOR(S): Liebaldt, G.
CORPORATE SOURCE: Univ.-Nervenklin., Wuerzburg, Germany
SOURCE: Arzneimittel-Forschung (1965), 15(9), 1056-60
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German

L16 ANSWER 126 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB Bivagotomized dogs and rabbits were pretreated with a total dose of 0.8 mg. of reserpine/kg. intramuscularly and 2-6 mg./kg. intravenously. The maximum ineffective dose of tyramine hydrochloride (I) after reserpine pretreatment was 96 γ/kg. in dogs and 226 γ/kg. in rabbits. In untreated dogs and rabbits the maximum ineffective dose was 15 and 42 γ/kg., resp. Intravenous injections of 1.0 g./dog and 75 mg./kg. of L-α-methyldopa into reserpine-pretreated dogs and rabbits, resp., increased the pressor responses to I, reaching a maximum in 1-2 hrs. Animals not pretreated with reserpine showed no changes in the pressor responses to I after equivalent doses of L-α-methyldopa. In reserpine-treated dogs and rabbits α-methyldopamine in intravenous doses of 0.2 and 2 mg./kg., resp., restored the activity of I but the maximum activity occurred within the 1st hr. and 2 and 6 γ of α-methylnorepinephrine/kg. in rabbits and dogs, resp. caused immediate increases in I responses. The pressor responses to I elicited by **norephinephrine** were less and of shorter duration than those of α-methylnorepinephrine. The effects of methyldopa are due to its amine metabolites. Particularly indicated is α-methylnorepinephrine as the mediator.
ACCESSION NUMBER: 1965:466153 CAPLUS
DOCUMENT NUMBER: 63:66153
ORIGINAL REFERENCE NO.: 63:12191h,12192a-b
TITLE: Restoration of tyramine pressor responses in reserpine-treated animals by methyldopa and its amine metabolites
AUTHOR(S): Pettinger, William A.; Spector, Sydney; Horwitz, David; Sjoerdsma, Albert
CORPORATE SOURCE: Natl. Heart Inst., Bethesda, MD
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1965), 118(4), 988-93
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 127 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB cf. CA 62, 13729g. The intravenous injection of amphetamine, 200 γ/kg. at 30-min. intervals, caused tachyphylaxis after the 5th dose but was not accompanied by any change in cardiac catechol amine levels. The injection of tyramine, 800 γ/kg. at 15-min. intervals, caused tachyphylaxis after the 9th dose as well as a significant decrease in catechol amine concentration as indicated by the accelerated fall in sp. activity of myocardial **norephinephrine** after injection of dl-norepinephrine-7-3H. After administration of amphetamine, tachyphylaxis to tyramine developed more rapidly and did not disappear with repeated doses of tyramine. Amphetamine, which did not interfere with the initial pressor response to tyramine nor with its release of norepinephrine from the heart, seems to act by blocking the entry of newly-synthesized norepinephrine into an easily released store of the compound

ACCESSION NUMBER: 1965:457556 CAPLUS
DOCUMENT NUMBER: 63:57556
ORIGINAL REFERENCE NO.: 63:10538a-b
TITLE: Pressor responses to amphetamine in the spinal cat and its influence on tachyphylaxis to tyramine
AUTHOR(S): Bhagat, B.
CORPORATE SOURCE: Howard Univ., Washington, D.C.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1965), 149(2), 206-11
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English

L16 ANSWER 128 OF 128 CAPLUS COPYRIGHT 2004 ACS on STN
AB A group of rats was injected with 0.5 ml. of 1.9 + 10-4 M **norephinephrine**-7-H3 and epinephrine-1-C14. The presence of tritium in the epinephrine and 3-methoxynorepinephrine zones indicates that norepinephrine is converted into epinephrine in vivo. The absence of C14 in the norepinephrine and 3-methoxynorepinephrine zones shows that epinephrine is not demethylated to norepinephrine, and the N-methylation of norepinephrine to epinephrine is an irreversible process in vivo. Epinephrine-H13 formed from norepinephrine-H3 is not o-methylated to the same extent as originally injected epinephrine-C14.

ACCESSION NUMBER: 1960:119728 CAPLUS
DOCUMENT NUMBER: 54:119728
ORIGINAL REFERENCE NO.: 54:22939d-f
TITLE: Relative metabolic rates of norepinephrine-7-H3 and epinephrine-1-C14
AUTHOR(S): Goldstein, M.; Friedhoff, A. J.; Sandler, G.
CORPORATE SOURCE: New York Univ., New York, NY
SOURCE: Experientia (1960), 16, 211
CODEN: EXPEAM; ISSN: 0014-4754
DOCUMENT TYPE: Journal
LANGUAGE: English

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=>  lofoff y
LOFOFF IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> logoff y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   660.05     667.72

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                  -166.60    -166.60

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